COMPARISON OF DELAYED CORD CLAMPING AND UMBILICAL CORD MILKING IN LATE PRETERM AND TERM INFANTS – AN OPEN LABEL RANDOMISED CONTROL TRIAL

Dissertation submitted to

THE TAMILNADU
DR.M.G.R. MEDICAL UNIVERSITY

in partial fulfilment of the requirements
for the award of the degree of

D.M. (NEONATOLOGY)

THE TAMILNADU
DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI

APRIL 2014

CERTIFICATE

This is to certify that the dissertation entitled **"COMPARISON OF DELAYED CORD CLAMPING AND UMBILICAL CORD MILKING IN LATE PRETERM AND TERM INFANTS – AN OPEN LABEL RANDOMISED CONTROL TRIAL"** is a bonafide work done by **Dr.S.BALAJI** under my guidance and supervision during the period between Nov 2013 – Feb 2014 towards the partial fulfilment of requirement for the award of **D.M. (Neonatology)** degree examination to be held in August 2014 by the Tamilnadu Dr. M.G.R. Medical University, Chennai.

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This is to certify that the dissertation entitled **"COMPARISON OF DELAYED CORD CLAMPING AND UMBILICAL CORD MILKING IN LATE PRETERM AND TERM INFANTS – AN OPEN LABEL RANDOMISED CONTROL TRIAL"** is a bonafide work done by Dr.S.Balaji., Madras medical college in partial fulfillment of the University rules and regulations for award of DM Neonatology under my guidance and supervision during the academic year 2011 – 2014.

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DECLARATION

I solemnly declare that this study titled **"COMPARISON OF DELAYED CORD CLAMPING AND UMBILICAL CORD MILKING IN LATE PRETERM AND TERM INFANTS – AN OPEN LABEL RANDOMISED CONTROL TRIAL"** was my original work in the Department of Neonatology, Madras medical college, Chennai under the guidance and supervision of Prof.J.Kumutha MD.,DCH., Professor & Head of the department, Department of Neonatology, Institute of child health and hospital for Children, Egmore, Chennai. This dissertation is submitted to The Tamilnadu Dr.M.G.R Medical University, Chennai in partial fulfilment of the university requirements for the award of the degree of D.M. Neonatology.

Place: Chennai
Date: **Dr.S.BALAJI**

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

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CERTIFICATE OF APPROVAL

To
Dr. S. Balaji,
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Dear Dr. S. Balaji,

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled **"Comparison of delayed cord clamping versus umbilical cord milking in late preterm and term infants – An open label randomized control trial"** No.21112013

The following members of Ethics Committee were present in the meeting held on 13.11.2013 conducted at Madras Medical College, Chennai-3.

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2. Prof. R. Nandini, MD Director, Instt. of Pharmacology, MMC, Ch-3	-- Member Secretary
3. Prof. Ramadevi, Director i/c, Instt. of Biochemistry, Chennai.	-- Member
4. Prof. P. Karkuzhali, MD Prof. Instt. of Pathology, MMC, Ch-3	-- Member
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6. Thiru. S. Govindasamy, BABL	-- Lawyer
7. Tmt. Arnold Saulina, MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

R Nandini

Member Secretary, Ethics Committee

MEMBER SECRETARY
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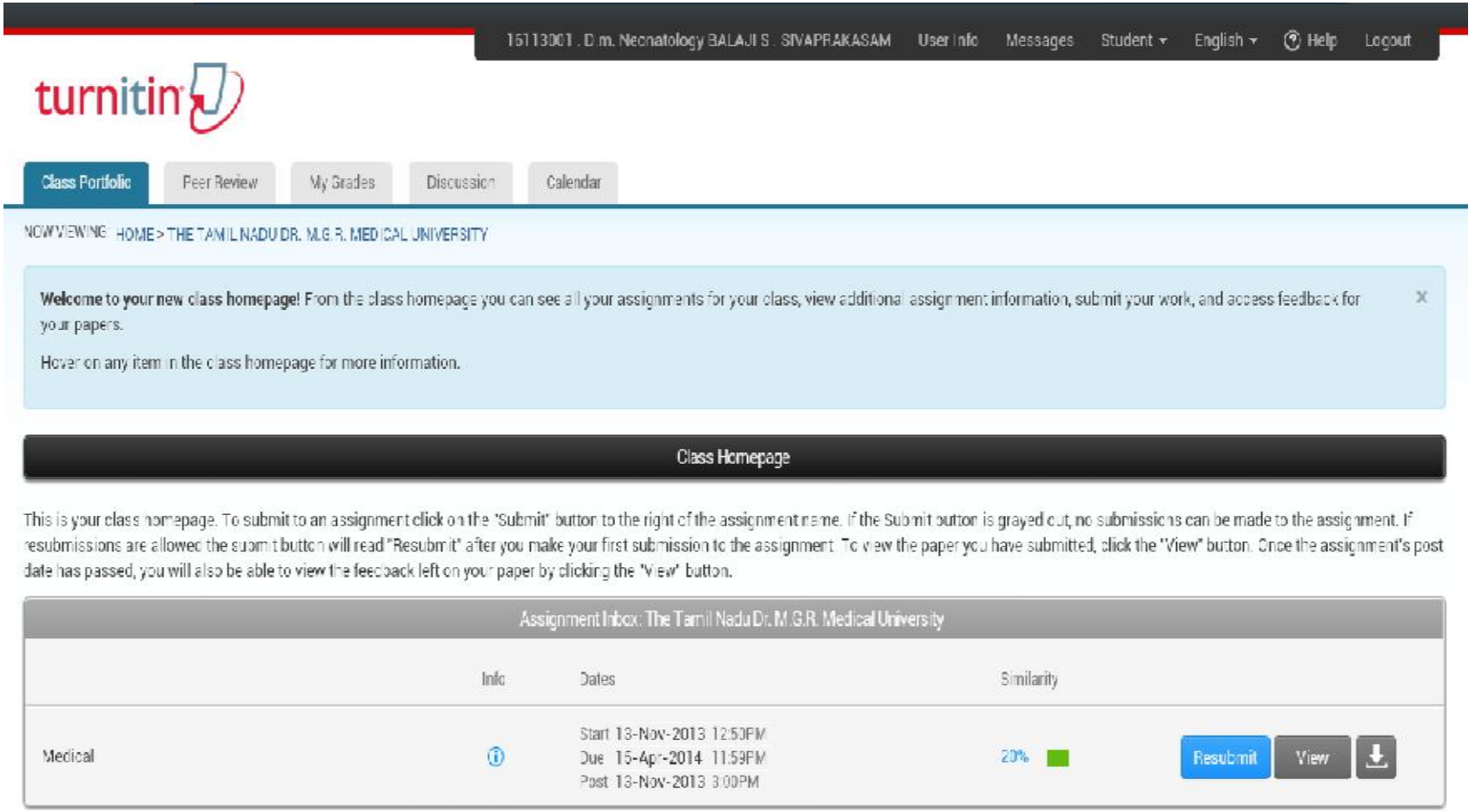
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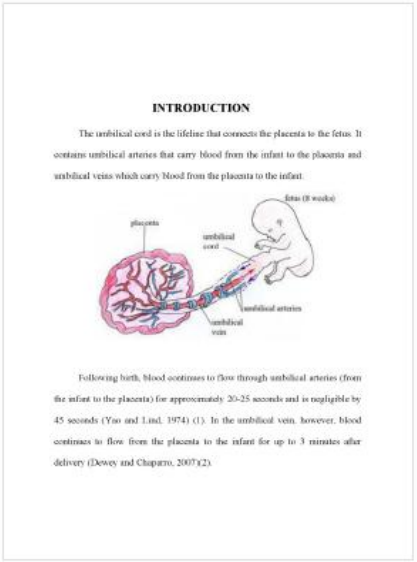

INTRODUCTION

The umbilical cord is the lifeline that connects the placenta to the fetus. It contains umbilical arteries that carry blood from the infant to the placenta and umbilical veins which carry blood from the placenta to the infant.

Following birth, blood continues to flow through umbilical arteries (from the infant to the placenta) for approximately 20-25 seconds and is negligible by 45 seconds (Yao and Lind, 1974) (1). In the umbilical vein, however, blood continues to flow from the placenta to the infant for up to 3 minutes after delivery (Dewey and Chaparro, 2007)(2).

CONTENTS

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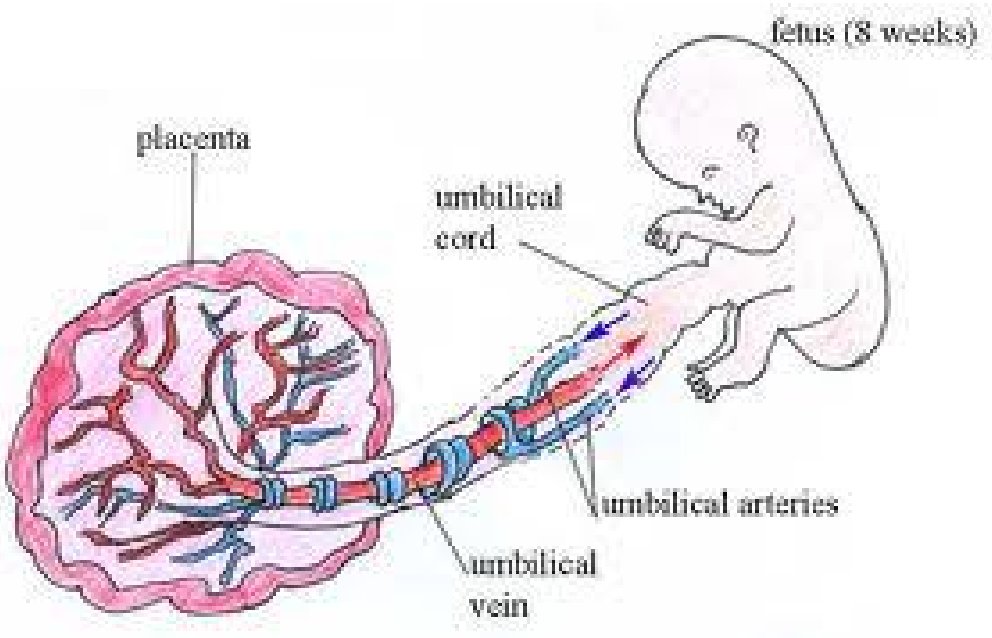

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This additional blood volume transferred from the placenta to the neonate at birth through the umbilical vein is defined as Placental transfusion (Duley *et al.*, 2009)(3). Placental transfusion is affected by three main factors namely uterine contractions following delivery, position of infant following delivery, and timing of umbilical cord clamping (Duley *et al.*, 2009) (3).

Active management of the third stage of labour includes administration of uterotonic agent, early cord clamping & cutting and controlled cord traction (Prendiville et al. 2000) (4). It has supplanted the 'physiological' approach; as a consequence the umbilical cord is usually clamped soon after delivery of the neonate.

The placenta contains approximately 100 ml of blood and the mean blood volume of a term infant is about 85 ml/kg. The interval between delivery and clamping of the umbilical cord can significantly affect a newborn's blood volume and total RBC mass. Early cord clamping reduces the placental transfusion and hence reduces mean blood volume by about 10%.

In FIGO- ICM definition (5) of active management of third stage of labour, early cord clamping is excluded based on research indicating

that delayed clamping benefits preterm and term infants (Van Rheenen et al 2006)(6).

One of the major advantages of delayed cord clamping is increase in circulating volume and haemoglobin level. Beard et al 2007 and Carlson et al 2009 in their study showed that the benefits of the delayed cord clamping include less respiratory distress and reduced need for later transfusions especially in preterm babies(7,8).

Increasing the hemoglobin level and iron stores are beneficial because anemia in early infancy is a frequent problem, especially in developing countries. However these potential benefits need to be balanced against possible harmful effects in infant (delayed resuscitation, hypothermia, polycythemia, hyperbilirubinemia and risk of intraventricular hemorrhage).

However, a recent meta analysis by Mathew et al 2011 reported that delayed cord clamping is beneficial in reducing anemia in term (15 RCTs) and preterm (14 RCTs) neonates. It improves the infant's iron stores, which may be of particular value in settings in which nutrition is poor (9). Hence delayed cord clamping has been recommended by various National and International organisations but it is not practised widely due to difficulty in implementation of this procedure.

An alternative method that could increase the placental transfusion is umbilical cord milking. A recent study by Amit Upadhaya et al demonstrated that umbilical cord milking is safe and it improves the haemoglobin and iron stores at 6 weeks of age when compared to delayed cord clamping (10).

Umbilical cord milking may be considered as an effective alternative to delayed cord clamping for improving the placental transfusion.

However, there are insufficient data about the effect of umbilical cord milking and delayed cord clamping in full-term and late preterm infants.

Our study is aimed to investigate the effect of umbilical cord milking compared with delayed cord clamping on haematological parameters at 2 months of age among term and late preterm infants.

Review of Literature

REVIEW OF LITERATURE

Hemoglobin levels during gestation and first year of life

Iron transport to the fetus occurs mostly during the third trimester of pregnancy (Bradley *et al.*, 2004) (11). Hemoglobin level is higher at birth than at any other period of life and reduces from approximately 17 gm/dl at birth to a low of about 11.2 gm/dl in the first two months of life (Brown, 1988) (12). This stage is referred to as the "physiological anemia of infancy" and is a result of the combined effect of the shorter lifespan of fetal erythrocytes, decreased red blood cell production and a dilution effect from increased blood volume related to growth (Brown, 1988) (12).

From 2 months onward, haemoglobin concentration increases slightly and usually reaches about 11.8 gm/dl by four to six months of age (Domellof *et al.*, 2001) (13). Accompanying changes in haemoglobin concentration during the first few months of infancy is a redistribution of total body iron. Estimated amount to of total body iron in newborn is approximately 260 mg. Of which 70% is in the form of hemoglobin, 24% is stored as ferritin and Myoglobin & Iron-containing enzymes constitute remaining 6% (Dallman *et al.*, 1993) (14).

By 4 months of age, although there is little change in total body iron content, the distribution changes significantly. Iron stores are utilized for growth and therefore ferritin stores reduces to approximately 12%,

iron in haemoglobin increases to approximately 76%, and iron in myoglobin and iron-containing enzymes increases to 12% (Dallman *et al.*, 1993) (14).

After 4 to 6 months of age, the breast-fed infant begins to receive exogenous sources of iron such that total body iron increases to approximately 420 mg (Dewey and Chaparro, 2007) (2).

Determinants of birth iron stores

Iron store in a neonate is largely determined by maternal iron status, gestational age of and birth weight of the neonate, (Chaparro, 2008) (15). Several longitudinal studies, including one randomized controlled trial on iron supplementation during pregnancy, have found that maternal anemia during pregnancy is associated with anemia during infancy (de Pee *et al.*, 2002; Kilbride *et al.*, 1999; Preziosi *et al.*, 1997; Colomer *et al.*, 1990) (21-24).

The effect of maternal iron deficiency during pregnancy on infant iron stores at birth, however, is controversial. Cross-sectional studies have produced conflicting results. This is likely due to variable degrees of iron deficiency in the women studied and differing attributes of the pregnancy and delivery that can alter the indicators used to assess anemia (Chaparro, 2008) (15).

The effect of birth weight on iron stores at birth is more well known. A linear relationship between body iron and birth weight exists such that birth iron stores increase with increasing birth weight (Widdowson and Spray, 1951).

Although gestational age is correlated with the amount of body iron stores at birth, the correlation between birth weight and gestational age may, to a large degree, account for this (Chaparro, 2008)(15). There is an increase in the total amount of iron stores in liver, because of an increase in liver size during the last eight weeks of gestation, which is related to birth size of neonate (Chaparro, 2008) (15).

Depletion of iron stores during first year of life

During the first six months of an infant's life, the optimal feeding practice is exclusive breastfeeding. Breastmilk, however, does not provide the infant with a significant amount of iron (Oski and Landaw, 1980) (16). The amount of iron absorbed from human breast milk is approximately equivalent to the amount of total iron lost (majority lost by sloughing of epithelial cells of the gastrointestinal tract) (Oski and Landaw, 1980) (16). Body iron stores at birth, therefore, are essential to ensure adequate iron levels and are required to sustain growth and development during the first six months of life (Chaparro, 2008) (15).

Low birth weight infants are at a higher risk of iron deficiency during the first six months of infancy because they begin life with lower iron stores and require more iron to sustain their faster rate of post-natal growth (Chaparro, 2008) (15). The high prevalence of anemia in six-to-nine months raises the concern that birth iron stores in some infants are insufficient to sustain growth and development through the first six months of life (Chaparro, 2008) (15).

Consequences of fetal / infant anemia

Iron is a critical nutrient for the normal development of brain (Lozoff and Georgieff, 2006) (17). The structures of the brain can become abnormal due to iron deficiency *in utero* or in early postnatal life, as iron is essential for proper neurogenesis and differentiation of certain brain cells and brain regions (Rao *et al.*, 2007; Ward *et al.*, 2007; Rao *et al.*, 2003) (18-20)

In the fetus, red blood cells receive priority for iron over other tissues including the brain (Lozoff and Georgieff, 2006) (17). When iron supply does not meet iron demand, as in the case of iron deficiency, the fetal brain may be at risk of developmental problems (Lozoff and Georgieff, 2006) (17).

Iron deficiency during infancy is associated with poorer cognitive, motor, and/or social and emotional outcomes later in life (Lozoff and

Georgieff, 2006) (17). What is particularly alarming regarding iron deficiency during early infancy is the finding that many negative consequences are not reversed following iron therapy (Lozoff and Georgieff, 2006) (17).

The best strategy to prevent and/or reverse adverse effects is to give iron therapy early before iron deficiency manifest (Lozoff and Georgieff, 2006) (17). This highlights the importance of prevention of fetal and infant iron deficiency.

Preventing iron deficiency anemia in infancy.

The optimal strategy to prevent iron deficiency in infancy is to scale up interventions with a record of evidence-based efficacy and effectiveness. There is an increasing need to translate research into cost-effective and sustainable programs. Four such interventions that are known to be effective in preventing iron deficiency during the first six months of life are iron supplementation to pregnant women, delayed umbilical cord clamping at birth, early initiation of breast-feeding and continued exclusive breast-feeding for six months (Stoltzfus et al 2008) (25).

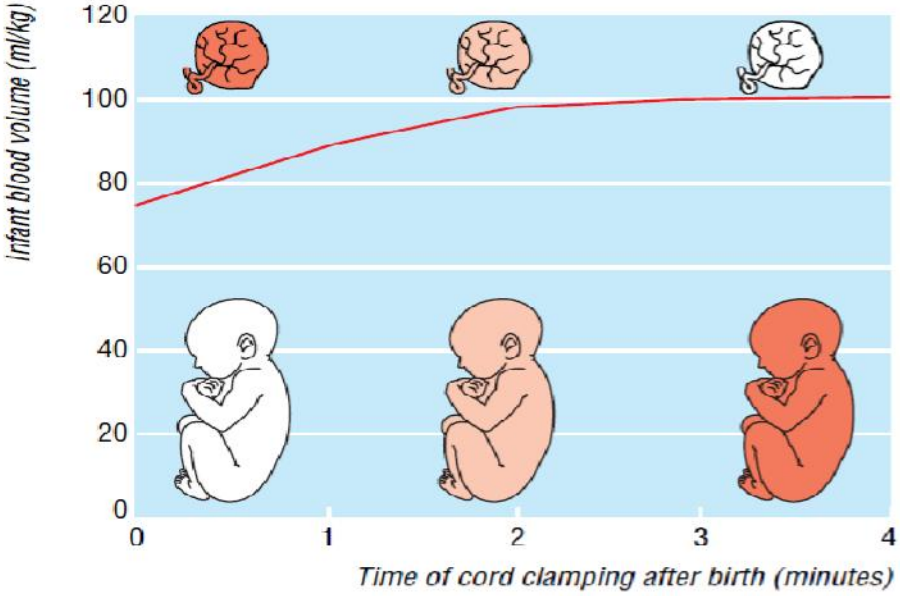
Umbilical cord clamping

Active management of third stage of labour became part of clinical practice following documentation of its effect in decreasing the risk of maternal postpartum hemorrhage by 50% compared to physiological management (Duley *et al.*, 2009; Enkin *et al.*, 2000) (26,27).

Recently, however, it has come to light that the beneficial effects of the individual components of active management of labour have not been adequately studied. The effect of decreased risk of post-partum hemorrhage observed following the active management of third stage of labour is almost entirely due to the use of utero tonic drugs and not the result of the three combined interventions as was originally thought. Following this realization, the impact of the timing of umbilical cord clamping has undergone intensive scientific investigation.

Placental transfusion

Placental transfusion is defined as the additional blood volume transferred from the placenta to the infant at birth through the umbilical vein (Duley *et al.*, 2009)(26). Placental transfusion is affected by three main factors: uterine contractions following delivery, placement of infant following delivery, and timing of umbilical cord clamping (Duley *et al.*, 2009)(26).



Distribution of blood between infant and placenta depending on time of cord clamping.

The timing of umbilical cord clamping will affect the amount of blood volume transferred to the infant through placental transfusion. Farrar et al estimated the placental transfusion in term infants by measuring infant weight gain in the first 5 minutes after birth while the cord was left intact at vaginal and cesarean birth. The mean amount of placental transfusion was 81ml (range 50 to 163ml) or 25ml/kg (range 16 to 45ml/kg). The authors estimated that placental transfusion contributed to about 20% of the infant's blood volume at birth (28).

Narenda et al was able to show that a brief delay (~30 to 45 seconds) in cord clamping in preterm infants resulted in a 8% to 24% increase in blood volume (2 to 16 ml/kg at cesarean delivery and 10 to 28ml/kg at vaginal delivery (29).

In one study of harvested placental blood, a residual volume of approximately 15 to 20 ml blood could often be obtained from the umbilical vein itself (30). When the cord is cut immediately, approximately 20ml/kg of infant whole blood and 25mg/kg of iron remains in the placenta and it is routinely discarded as medical waste after birth (31, 32).

During placental transfusion, an additional 15-40 ml/kg birth weight of blood volume is transferred from the placenta to the infant through the umbilical cord. Therefore, waiting to clamp the umbilical cord and allowing placental transfusion to complete can increase a term neonate's blood volume by approximately 30-50% (Levy and Blickstein, 2006; Dewey and Chaparro, 2007). Approximately 25% of the transfer occurs in the first 15 – 30 seconds after birth, 50-78% of the transfer by one minute and the remaining by three minutes (Yao *et al.*, 1969) (31).

Thus the timing of umbilical cord clamping will affect the extent of placental transfusion. Obviously, placental transfusion cannot occur if the umbilical cord is clamped or cut, blocking or severing the link between the infant and the placenta. Delaying umbilical cord clamping until placental transfusion can be completed will maximize the blood volume transfused to the infant. Providing the neonate with additional blood

volume by delaying umbilical cord clamping has many subsequent effects on child Health outcomes.

Effects of delayed cord clamping in term infants

A number of systematic reviews (McDonald et al., 2008, Hutton et al., 2007, Mathew et al., 2007) have examined the risks and benefits of delayed cord clamping in healthy term infants. These have found an increase in hemoglobin concentration and improved iron status up to six months after birth, thus decreasing the risk of early neonatal anemia and iron deficiency (33,34,35,9).

The increase in neonatal blood volume has the potential not only to increase iron stores and haemoglobin concentrations but also to augment jaundice . In a recent Cochrane review, risk between Early cord clamping and delayed cord clamping for the development of jaundice requiring phototherapy was significantly higher in the delayed cord clamping group (34).

Conversely, two separate systematic reviews by Mathew et al and Rabe et al found no significant difference in mean serum bilirubin, development of neonatal jaundice, or requirement for phototherapy between these groups (35,9).

However, the conclusions of Andersson et al (33) the most recent and one of the largest studies evaluating neonatal outcomes after delayed

cord clamping, are promising and strengthen the belief that Delayed cord clamping does not increase the risk of hyperbilirubinemia. Apart from this insignificant risk of jaundice and need for phototherapy, Delayed cord clamping has not been shown to affect other neonatal outcomes negatively in term infants. Specifically, there are no differences in Apgar scores at five minutes, rates of NICU admission, or rates of respiratory distress in comparisons of Early cord clamping and delayed cord clamping in healthy term infants (33,34,35,9).

Delayed cord clamping presents a number of clinically relevant benefits, with minimal risk if any. These include decreasing neonatal anemia and iron deficiency, which may have a positive impact on development. These advantages are also present in populations in which iron deficiency has a relatively low prevalence (33). Therefore, a universal approach to delayed cord clamping in the term infant can be justified, given the current available evidence.

Effects of delayed cord clamping in preterm infants.

The issue of cord clamping in preterm infants is more controversial than in term infants because many clinicians fear that delaying cord clamping may interfere with resuscitation in this more vulnerable population. Many studies show that there are several advantages to delaying cord clamping by more than 30 seconds in preterm infants.(9,36-

38). Importantly, doing so neither affect their Apgar scores significantly, nor does it increase the risk of other neonatal outcomes such as respiratory distress, jaundice requiring phototherapy, and mortality.(9,36).

The benefits of delayed cord clamping in this population include decreasing the need for and the number of blood transfusions for anemia by increasing blood volume RR 0.72(95% CI 0.54, 0.96) and hematocrit at birth MD 3.04 (2.58, 3.51), decreasing the risk of intraventricular hemorrhage RR0.49 (95% CI-0.32, 0.74) and decreasing the risk of late onset sepsis.(9,36-38).

Current practices of timing of umbilical cord clamping

One recent study attempted to describe current practices of the timing of umbilical cord clamping across Europe (Winter *et al.*, 2007) (39). This study concluded that 66-90% of maternity units in Belgium, France, Italy, the Netherlands, Portugal, Spain, Switzerland, and the UK had policies of clamping and cutting the cord immediately after birth (Winter *et al.*, 2007) (39).

Conversely, 65-74% of maternity units in Austria, Denmark, Finland, Hungary, and Norway had policies of waiting until the cord stopped pulsating (Winter *et al.*, 2007) (39).

There did not appear to be any demographic determinants of timing of cord clamping and many respondents implied that practice was dictated by institutional policies, independent of their own beliefs (Mercer *et al.*, 2000)(40). The high degree of variability in the timing of cord clamping found in these studies reflects an inadequate scientific knowledge base among obstetric staff.

Attitudes of health professionals towards delayed cord clamping

A questionnaire-based study published in 2009 attempted to investigate the attitudes of obstetricians towards delayed cord clamping (Ononeze and Hutchon, 2009) (18). They concluded that only 9.3% of obstetricians sampled from hospitals across the British Isles, European countries, USA, Canada, Australia, etc. always adhere to recommendations on delayed umbilical cord clamping (Ononeze and Hutchon, 2009) (41). Reasons for non-adherence include difficulty implementing delayed cord clamping in clinical practice and being unaware of the scientific evidence (Ononeze and Hutchon, 2009) (41).

When 303 certified American nurse-midwives were randomly sampled from all active members of the American College of Nurse-Midwives and asked to complete a questionnaire, 21% reported that they clamp the cord immediately, 5% clamp before one minute, 35.7% clamp

between one to three minutes, 3.8% clamp after three minutes, and 29.3% clamp after cord pulsations have ceased (Mercer *et al.*, 2000) (40).

Effects of Umbilical cord milking

Umbilical cord milking is the another method of increasing the placental transfusion in which cord is milked several times towards the baby from the placenta. It has also shown same beneficial effects as that of the delayed clamping, in which waiting for few minutes is not needed.

The largest body of evidence describing umbilical cord milking comes from studies published in the middle of the 20th century (1940's-1960's) using this methodology and reporting styles that do not meet contemporary standards. These studies (Archilei 1960; Colozzi 1954; McCausland 1949; Siddal 1952; Siddal 1953; Whipple 1957) describe consecutive series of primarily full- term, healthy newborns assigned in a non-randomized or quasi-randomized method to immediate cord clamping or cord milking. None of these published studies described any adverse effects from cord milking.

Hosono & coworker demonstrated that umbilical cord milking resulted in a higher blood pressure and urine outputs during the first 12 hours of life, shorter duration of assisted ventilation and less need for blood transfusion (42,43).Umbilical cord milking results in placental transfusion in term infants at the time of cesarean section with higher

hematocrit at 36-48 hours of life (Erickson et al 2011) (44). Umbilical cord milking is a safe procedure and shows improved Hemoglobin and iron status at 6 weeks of life among term and near term neonates (Amit Upadhayay et al 2013) (10).

Delayed cord clamping versus milking

Rabe et al who compared these two techniques of delayed cord clamping and umbilical cord milking concluded that in preterm infants milking the cord four times achieved a similar amount of placento-fetal blood transfusion compared with delaying clamping the cord for 30 seconds (45). At present there are no studies comparing these two techniques in late preterm and term neonates.

Milking of the umbilical cord may be an alternative strategy for increasing placental transfusion in the preterm baby. In a recent study done by Rabe et al, milking the cord and Delayed cord clamping led to similar results in terms of haemoglobin concentration, need for transfusions, and other secondary outcomes such as intraventricular haemorrhage, sepsis, necrotizing enterocolitis, and death (45).

Justification

Delayed cord clamping in both preterm and term infants has been shown to be beneficial in improving the haemoglobin and iron status by increasing the placental transfusion in various studies and it is

recommended by various National and International organisations including World Health Organisation, but it is not practised widely. Difficulty in implementation at field level was the main reason for failure to adopt this recommendation. Obstetricians show reservations in adopting this recommendation.

Another technique which can improve the placental transfusion is milking of the Umbilical cord several times towards the baby and studies has shown the beneficial effects of milking when compared to immediate cord clamping in improving the placental transfusion in both preterm and term infants.

Milking the umbilical cord may be an effective alternative technique in increasing the placental transfusion easy to adopt and it can be completed within few seconds to achieve the same effects as that of the delayed cord clamping**.** Our study is aimed to compare the effects of delayed cord clamping at 2 minutes of life and milking of the umbilical cord 4 times towards the baby.

Hypothesis and Objectives

HYPOTHESIS AND OBJECTIVES

Hypothesis:

Milking of the umbilical cord 4 times, towards the baby from the placenta at the time of delivery both in caesarean and vaginal delivery is non inferior than delaying the clamping of umbilical cord at 2 minutes of life in improving the placental transfusion as measured by haemoglobin, hematocrit and serum ferritin without causing significant difference in adverse effects such as the respiratory distress, jaundice requiring phototherapy and Polycythemia, in preterm infants ≥34 weeks of gestational age and term infants.

Objectives of the Study

Primary Objective: To compare the level of Haemoglobin at 2 months of age in term infants and preterm infants ≥ 34 weeks gestation between Delayed cord clamping and Umbilical cord milking.

Secondary Objectives: To compare the following Hemodynamic, Haematological and Clinical parameters between the Delayed cord clamping and Umbilical cord milking after delivery.

1. Hemodynamic parameters-
    a. Heart rate - recorded by the auscultation of precordium for one full minute.
    b. Respiratory rate - recorded by clinical observation of movement of chest wall for one full minute.
2. Clinical parameters –
    a. Respiratory distress as measured by DOWNES score.
    b. Polycythemia defined as the venous hematocrit ≥65%.
    c. Jaundice requiring phototherapy.
3. Hematological parameters-
    a. Hemoglobin measured in venous blood using the cell counter
    b. Hematocrit measured in venous blood using the cell counter
    c. Serum bilirubin level measured by Diazo method.
    d. Serum ferritin level measured by Turbidometric method.

OUTCOME:

Primary Outcome:

To assess the level of haemoglobin at 2 months of age.

Secondary Outcome:

Assessment of

1. Hemodynamic parameters - Heart rate, Respiratory rate at 30 minutes and at 48 hours of life.
2. Clinical parameters - Respiratory distress at 30 minutes, Polycythemia, and Jaundice requiring phototherapy at 48 hours.
3. Hematological parameters- Hemoglobin, Hematocrit & serum bilirubin level at 48 hours and Hematocrit & serum ferritin at 2 months of age

Materials and Methods

MATERIALS AND METHODS

Study design:

Open label randomized controlled trial with the non inferiority framework.

Study site:

Study was conducted in Institute of Obstetrics and Gynaecology and Hospital for women and children in Chennai, Tamilnadu.

Study period:

November 2013 to February 2014

Subjects:

All neonates ≥34 weeks born either by vaginal route or through Lower segment caesarean section were considered eligible for the study.

Inclusion criteria:

All neonates ≥34 weeks of gestation delivered either by Lower Segment Caesarean section or Vaginal delivery during the presence of trained person for intervention and families living in proximity (within 20 km radius) of the institution were included in the study.

Exclusion Criteria:

Mother fetus pair with following characteristics were excluded from the study

- Multiple gestation,
- Rh negative mother,
- Baby limp at birth,
- Antenatally diagnosed major congenital malformation,
- Hydrops fetalis,
- Placenta previa,
- Placental abruption
- Maternal transfusion for anemia.

Sample size:

In the study conducted by Amit Upadhyay et al, late preterm and term infants who underwent umbilical cord milking had a mean haemoglobin of 11.9(+/- 1.5) gm% at 6 weeks. This was used for sample size calculation. It was used for sample size calculation. To detect 1 gm% difference (non inferiority margin) in haemoglobin at alpha of 0.05 and 90% power for two sided test, we needed to enrol 80 subjects (40 in each group). Since study was planned to be conducted on healthy babies, we anticipated a dropout rate of 20%, the determined sample size was 48 in each group.

Methodology

Gestational age assessment

Gestational age was calculated from the first trimester ultrasound dating and if it was not available last menstrual period was used.

Consent and ethical clearance

Informed written consent for the study was obtained from the pregnant mother for enrolment into the study after explaining about the study. They were also provided with the participant information sheet.

The study was approved by the institutional Ethical committee (No.21112013).

Randomisation:

Randomisation was done through computer generated random numbers placed in serially numbered opaque envelops. Eligible mothers admitted in the maternity hospital were randomized just before delivery into Group-1 (Delayed clamping group) or Group-2 (Umbilical cord milking group).

Interventions:

Delayed cord clamping:

After delivery, babies were positioned between the mother's thighs (for babies delivered through vaginal route) or on the mother's thigh (for babies delivered by caesarean section) umbilical cord was clamped and

cut 2-3 cm distance from the umbilical stump at 2 minutes of life. The timing of delayed clamping at 2 minutes was measured by a stop clock.

Umbilical cord milking:

After delivery, babies were positioned between the mother's thighs (for babies delivered through vaginal route) or on the mother's thigh (for babies delivered by caesarean section) and then available length of the umbilical cord was milked 4 times towards the baby from the vaginal introitus in case of vaginal delivery or from the abdominal wound in case of caesarean delivery, at a speed of 10 cm / sec and cord was clamped and cut 2 – 3 cm from umbilical stump.

Delayed cord clamping procedure

Umbilical cord milking procedure

According to our local protocol, after delivery, intramuscular oxytocin was given to vaginally delivered mother and intravenous oxytocin was given to mother who was delivered through caesarean section. All neonates were managed as per our unit protocol.

Measurement of outcomes:

The following parameters were recorded after intervention

At birth respiratory distress was assessed using DOWNES score. Neonates with DOWNES score of ≥2 were admitted in the newborn nursery for further management.

At 30 minutes of life, heart rate was recorded by the auscultation of precordium, respiratory rate was recorded by observation of chest wall movement over one full minute.

At 48 hours of life again heart rate and respiratory rate were recorded. One ml of venous sample was obtained from the baby for estimation of haemoglobin and hematocrit using Sysmex KX 21 cell counter and serum bilirubin level was assessed by Diazo method using ROBONIK semianalyzer.

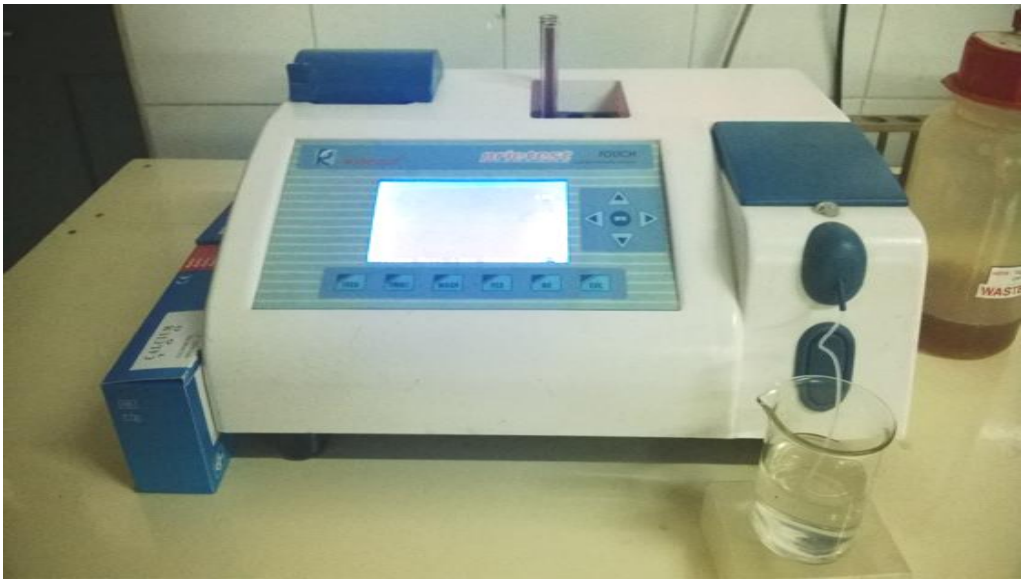
Baby was diagnosed to have polycythemia when the venous hematocrit recorded was ≥65%. Babies were started on phototherapy when their serum bilirubin level were in the phototherapy range. (As per AAP bilirubin nomogram)

All the study neonates were daily assessed for clinical jaundice till discharge and serum bilirubin was measured if clinical assessment of jaundice was significant. Babies were treated with phototherapy if the serum bilirubin levels were in phototherapy range. Peak serum bilirubin was measured.

Babies were discharged home as per our hospital protocol and they were followed up at secondary end point which was at 2 months of age.

On follow up at 2 months of age, haemoglobin, hematocrit and serum ferritin were estimated using venous blood. Serum ferritin was assay was done by Turbidometric method.

Serum bilirubin estimation semi analyser



Complete blood count cell counter

Serum ferritin kit

Serum ferritin estimation by Turbidometric method

Data collection:

Baseline parental data and neonatal data were recorded in the data collection sheet. Post intervention clinical, hematological and hemodynamic parameters were recorded in the data collection form. All the data were uploaded into the excel sheet (Microsoft excel 2008) at regular intervals. Infants were followed up till 2 months of age. No medicinal iron was given to any of these infants till the end of the study.

Statistical analysis:

Standard statistical tests were employed. Categorical variables were analysed with chi square test and continuous variables were analysed using student's independent t test. Results on continuous measurements were presented as Mean ± SD and results on categorical measurements were presented in percentage (%). P value of <0.05 was taken as significant. All statistical tests were two tailed tests. SPSS version 16.0 was used for data analysis.

Results and Analysis

RESULTS AND ANALYSIS

A total of 457 mothers were admitted for delivery during the study period. Of which 155 mothers were eligible for the study. Three hundred and five mothers were not eligible for reasons like Preterm delivery less than 34 weeks (65), Home distance more than 20 km radius (74) and trained persons not available for intervention (163).

Out of 155 eligible mothers 52 mothers were excluded. The reasons for exclusion were refusal of consent (38) ,Multiple gestation (2), Rh negative mother (6), Placenta previa (2), Abruptio placenta (1) and Mother received transfusion for anemia (3).

Totally 103 three mothers were enrolled and they were randomized to Delayed cord clamping group (n=52) and Umbilical cord milking group (n=51). Of 103 mothers enrolled, interventions were given only for 96 neonates.

Seven neonates (3 in Delayed clamping group and 4 in Milking group) were not intervened because they were limp at birth and required immediate resuscitation.

Flow diagram of study

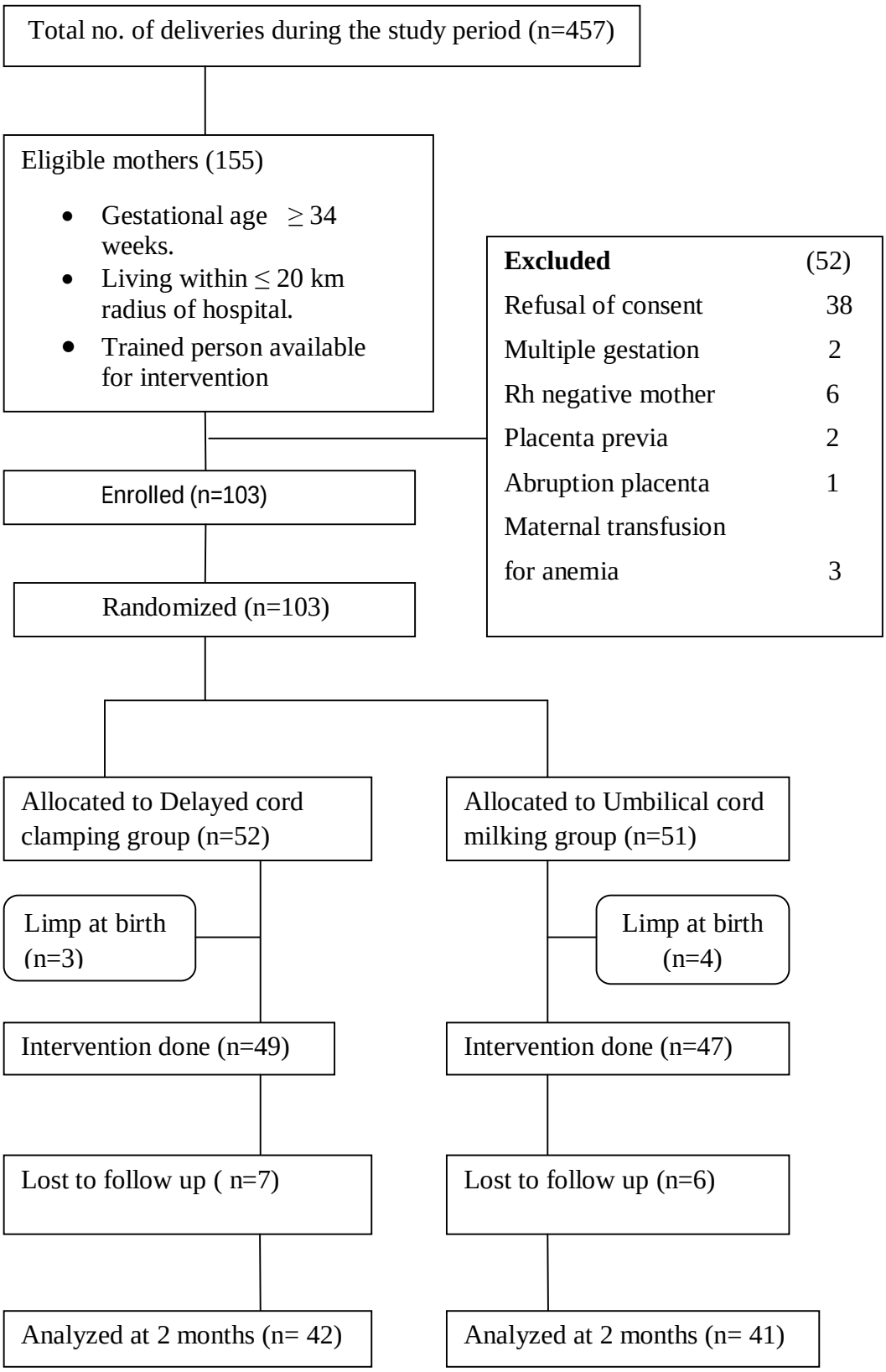


Fig: 1

Table : 1 - Baseline maternal characteristics

Characteristics	Delayed clamping (n=49)	Milking (n=47)	P value
Maternal age (yrs)	25.5 (±4.1)	25.6 (±4.2)	0.920
Maternal weight	65.1 (±9.9)	67.8 (±11.2)	0.220
Maternal Hb%	10.4 (±1.1)	10.4± (0.9)	0.776
Maternal anemia Hb% <11gm/dl*	35 (71.4)	38(80.9)	0.400
Maternal Hb%*			
<9 gm/dl	1 (2)	1 (2.1)	0.556
9-11 gm/dl	34 (69.4)	37 (78.7)	
≥11 gm/dl	14 (28.6)	9 (19.1%)	
Iron supplementation *	49 (100)	47(100)	1.000
Parity*			
Primi	18 (36.7)	18 (38.3)	1.000
Multi	31 (63.3)	29 (61.7)	
Mode of delivery*			
Vaginal	19 (38.8)	16 (34)	0.788
LSCS	30 (61.2)	31 (66)	
Oxytocin use*	49 (100)	47 (100)	1.000
Socio economic status * (Kuppusamy scale)			
1	0	0	
2	09 (18.4)	10 (21.3)	0.931
3	32 (65.3)	30 (63.8)	
4	08 (16.3)	07 (15)	
5	0	0	

Mean (SD), * No. (%).

Baseline maternal characteristics like age, weight, haemoglobin level, anemic status, parity, antenatal iron supplementation, mode of delivery and socioeconomic status were comparable between the two groups (Table-1)

Baseline maternal characteristics:

Distribution of Parity

There were no significant difference in number of babies born to Primi mothers and Multiparous mothers between the Delayed Clamping group and Milking group (p value 1.000).

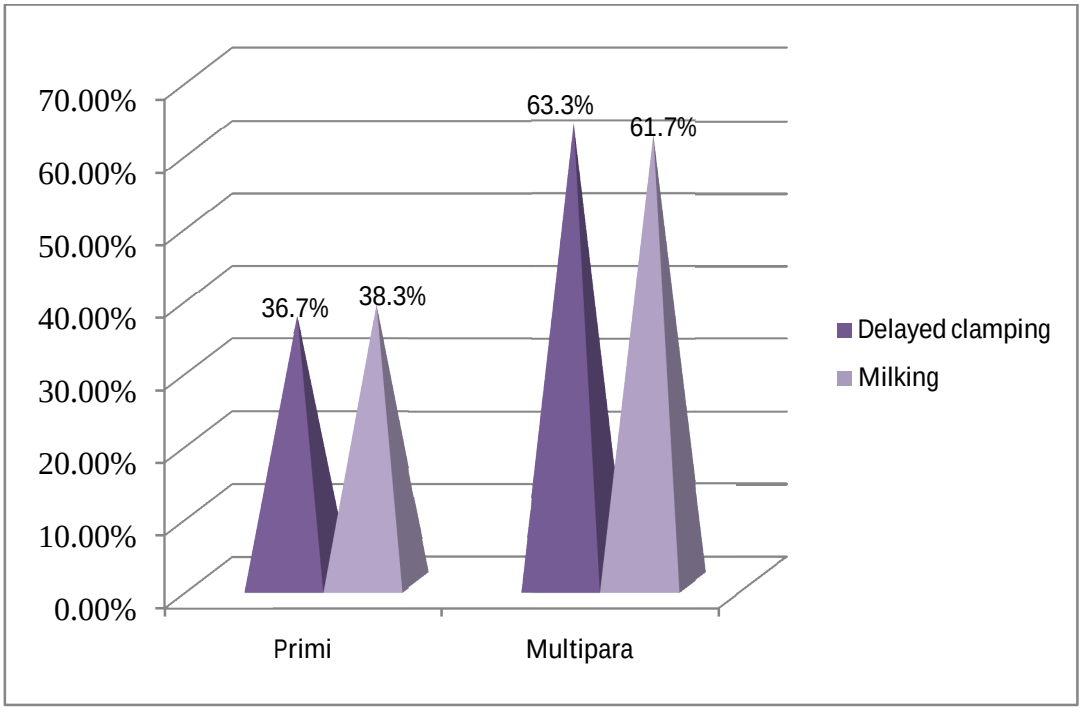


Fig 2: Parity of the mother in both the groups.

Mode of delivery

Most of the neonates included in the study were born through lower segment caesarean section (61.2% in Delayed clamping group and 66% in Milking group). 38.8% of neonates in delayed clamping group and 34% of neonates in milking group were delivered by vaginal route. There was no significant difference in mode of delivery between the two groups (P value 0.788).

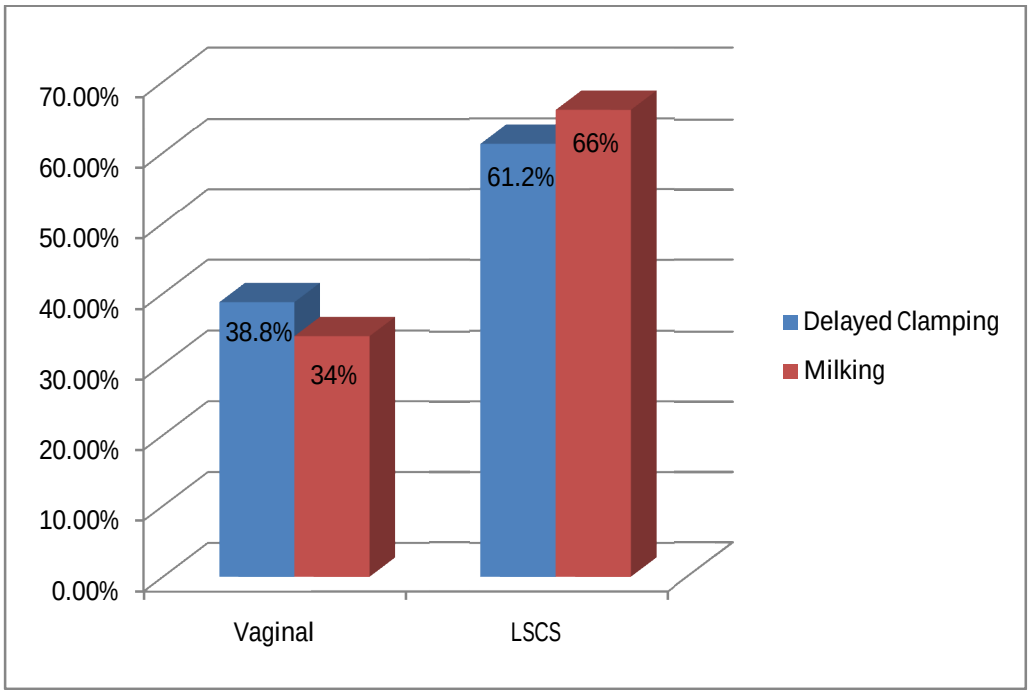


Fig 3: Mode of delivery of neonates in both the groups

Socio Economic status of parents

Most of the mothers in this cohort were under grade 3 socio economic status (Kuppusamy scale). 65.3% of mothers in delayed clamping group and 63.8% of mothers milking group were belong to grade 3 socio economic status. Mothers in all the classes of socio economic status in both delayed clamping and milking were comparable and P value (0.931) was statistically not significant.

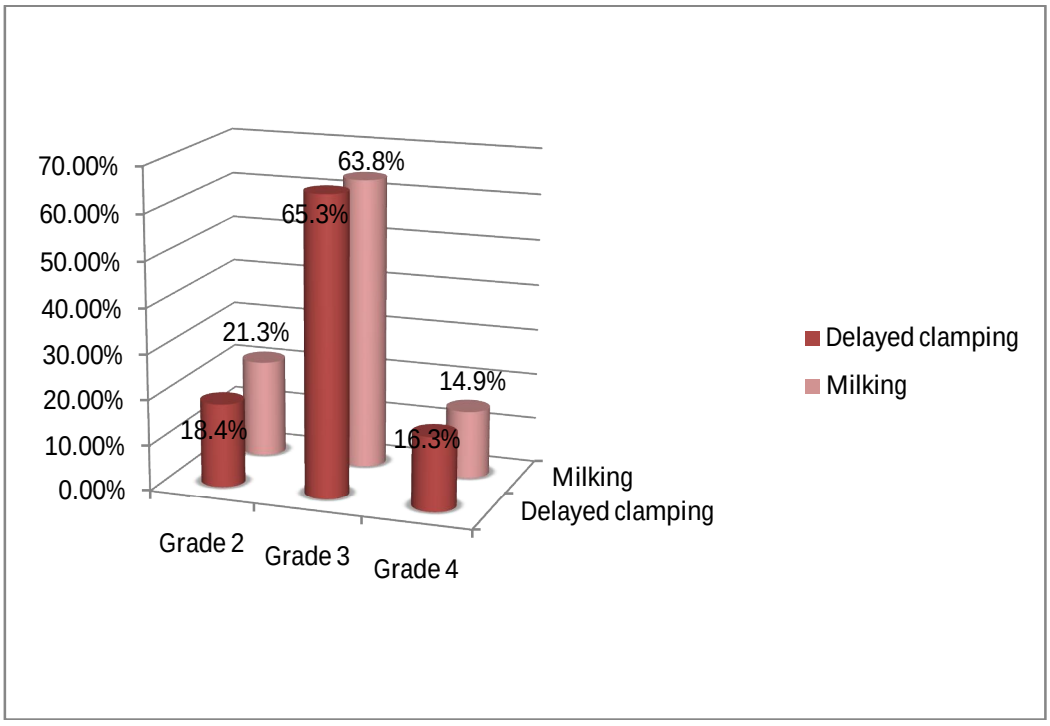


Fig 4: Socio economic status of parents in both the groups

Table: 2 - Baseline Neonatal characteristics

Characteristics	Delayed clamping (n=49)	Milking (n=47)	P value
Birth weight (grams)	3058.4 (±483.5)	2951.3 (±497.5)	0.288
Sex - Male *	23 (47)	24(51)	0.842
Gestation age in weeks	38.7 (±1.5)	38.5 (±1.5)	0.458
Gestation age *			
37-42 weeks	42 (±85.7)	40 (±85.1)	1.000
34-37 weeks	7 (±14.3)	7 (±14.9)	
Growth status *			
AGA	45(±91.8)	44 (±93.6)	1.000
SGA	4 (±8.2)	3 (±6.4)	
LGA	0	0	

Mean (SD), *No. (%).

Baseline neonatal characteristics like mean birth weight, Sex, Gestational age and growth status were comparable between the two groups (Table – 2)

Gestational age of neonates

Most of the neonates in this study were term neonates (42 were in Delayed clamping group and 40 neonates were in Milking group). Preterm neonates with gestational age ≥34 weeks were seven neonates in each group. Both the groups were comparable.

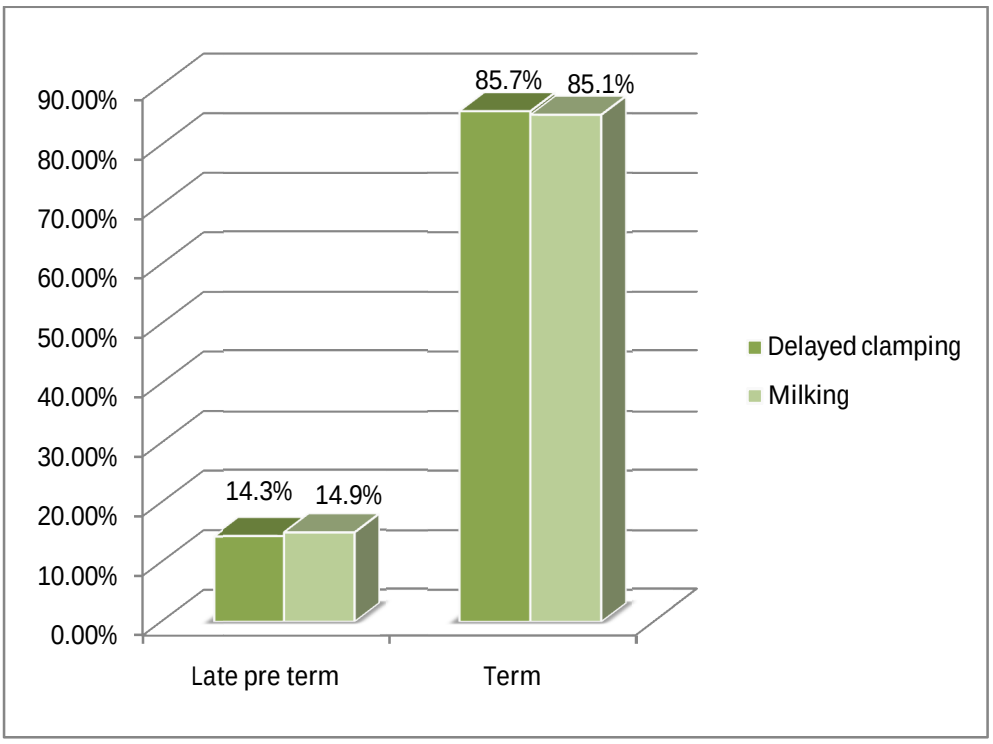


Fig 5: Gestational age in both the groups

Growth status of neonates

In Delayed cord clamping group, AGA and SGA neonates were 91.8% and 8.2% respectively and in milking group, AGA and SGA neonates were 93.6% and 6.4% respectively. Both the groups were comparable with P Value of 1.000. There were no LGA neonates in both the groups.

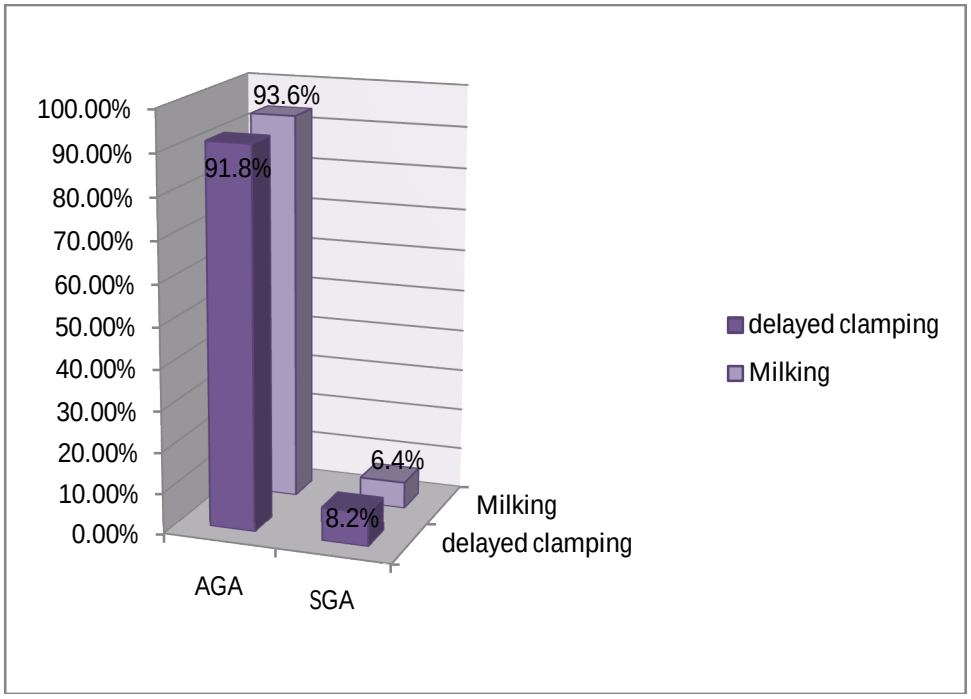


Fig 6: Growth status in both the groups

Primary outcome

Table : 3 - Haemoglobin level at 2 months of age in both groups.

Primary outcome	Delayed clamping (n=42)	Milking (n=41)	P value	Mean difference	95% CI
Hb%	12.7 (±1.4)	12.4 (±1.4)	0.490	0.3	-0.4 to 0.8

Mean (SD)

We did not find any significant difference in mean haemoglobin level between delayed cord clamping group and umbilical cord milking group at 2 months of age as depicted in the Table 3. Mean difference in haemoglobin was 0.3 gm/dl. It was statistically not significant (p value 0.490). Ninty five percent confidence interval (CI) was between -0.4 to +0.8 gm/dl.

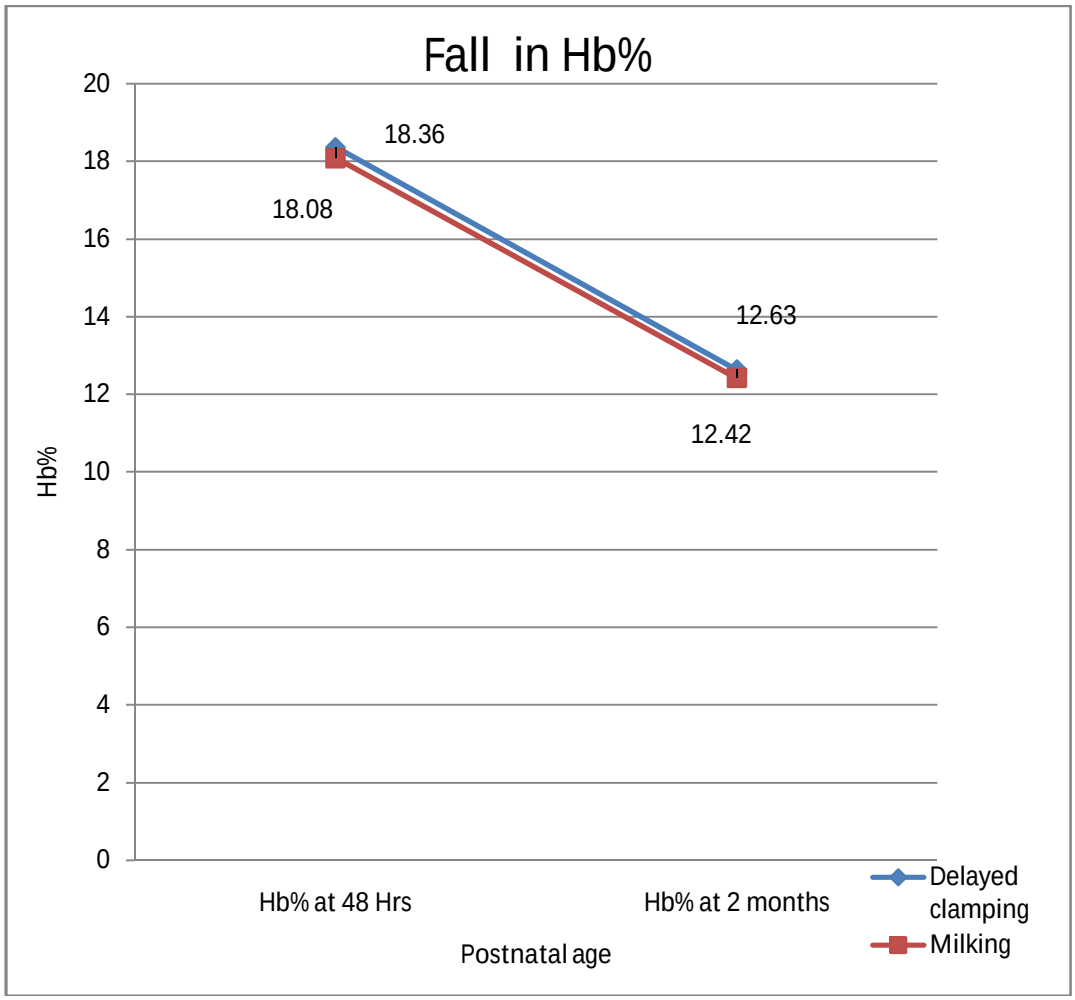


Fig 7: Haemoglobin level in two groups at 48 hours and 2 months

Post natal fall in haemoglobin level from 48 hours to 2 months of age in delayed cord clamping and umbilical cord milking groups were comparable as depicted in figure 7.

Sub group analysis for primary outcome

Table : 4 - Hemoglobin level at 2 months

Gestational age	Delayed cord clamping (n=42)	Umbilical cord milking (n=41)	P value	95% CI
Late preterm	12.5(±1.5)	12.7 (±0.4)	0.825	-1.77 to 1.45
Term	12.6 (±1.4)	12.4 (±1.5)	0.437	-0.41 to 0.94

Mean (SD)

In late preterm and term neonates there was no significant difference in Mean haemoglobin level at 2 months between the two groups as shown in table.4

Table : 5 - Mean Hemoglobin level at 2 months

Mode of delivery	Delayed cord clamping (n=42)	Umbilical cord milking (n=41)	P value	95%CI
Vaginal	12.9 (±1.2)	12.8 (±1.3)	0.777	-0.82 to 1.08
LSCS	12.5 (±1.5)	12.3 (±1.5)	0.063	-0.62 to 1.01

Mean (SD)

With regarding to mode of delivery there was no significant difference in mean haemoglobin level between the two groups at 2 months of age.

Secondary outcome

Table : 6 - Hemodynamic parameters within 48 hours

Parameters	Delayed group (n=49)	Milking group (n=47)	P value	Mean Difference	95% CI
RR at 30min	52.4 (±5.6)	51.8 (±4.9)	0.575	0.6	-1.5 to 2.8
RR at 48 hrs	48.2 (±4.1)	49.2 (±4.6)	0.282	1.0	-2.7 to 0.8
HR at 30min	147.3 (±9.0)	145.0 (±10.7)	0.264	2.3	-1.7 to 6.3
HR at 48 hrs	142.1 (±11.2)	144.7 (±11.4)	0.272	2.6	-7.1to 2.0

Mean (SD)

At 30 minutes and at 48 hours of life, no significant differences were observered in heart rate and respiratory rate between Delayed cord clamping and Umbilical cord clamping group. None of the neonates had tachycardia within first 48 hours of life in both the groups.

Table : 7 - Clinical parameters within 48 hours of life

Parameters	Delayed group (n=49)	Milking group (n=47)	P value
Respiratory distress at birth*	3(6.1%)	2(4.3%)	1.000
Need for Phototherapy*	5(10.2%)	5(10.6%)	
Polycythemia*	0	0	

*no(%)

Regarding clinical parameters like number of neonates required admission for respiratory distress and significant jaundice requiring phototherapy, there was no significant difference between the two groups. Approximately 10% of the neonates in Delayed clamping group and Milking group required phototherapy for hyperbilirubinemia. No polycythemia was detected in either group.

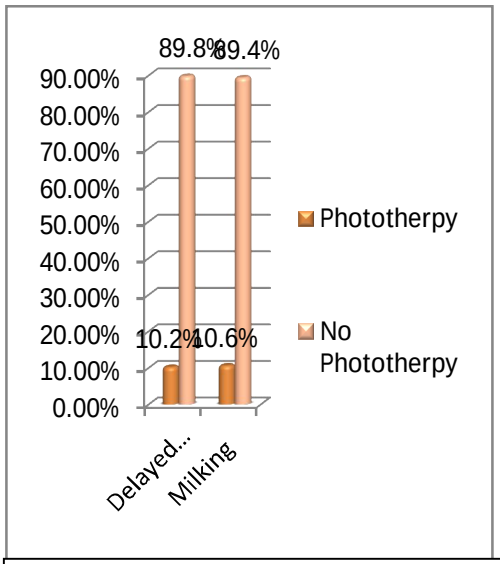


Fig 8: Need for phototherapy

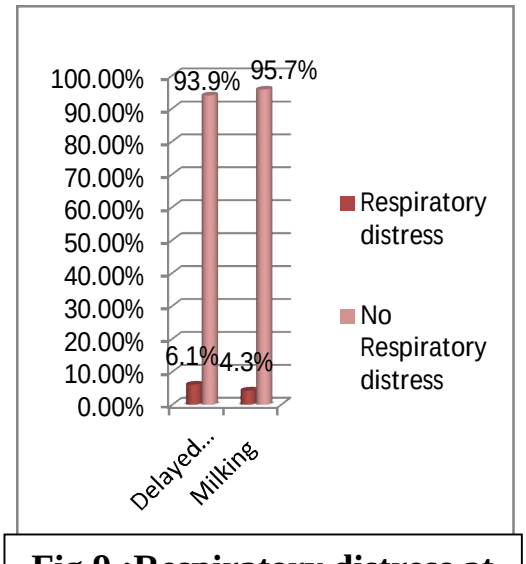


Fig 9 :Respiratory distress at birth

Table : 8 - Peak Bilirubin (Among the babies admitted for phototherapy)

	Delayed cord clamping (n=5)	Umbilical cord milking (n=5)	P value
Peak Bilirubin in mg%	16.2 (±0.8)	16.1 (±0.6)	0.735

Mean (SD)

Among the neonates who was underwent phototherapy, there was no significant difference in peak mean serum bilirubin levels between the two groups.

Table : 9 - Hematological parameters at 48 hours of life

	Delayed group (n=49)	Milking group (n=47)	P value	Mean Difference	95% CI
Hb % at 48hrs	18.4(±1.6)	18.9(±1.7)	0.404	0.5	-0.4 to 0.9
Hct at 48hrs	53.2(±4.5)	52.8(±4.8)	0.731	0.4	-1.6 to 2.2
SBR at 48 hrs	8.9(±3.6)	8.8(±4.3)	0.881	0.1	-1.5 to 1.7

Mean (SD)

The mean haemoglobin, hematocrit and serum bilirubin levels at 48 hours of life were comparable in both groups. The mean difference in haemoglobin, hematocrit and serum bilirubin was 0.5mg/dl, 0.4mg/dl and 0.1mg/dl respectively.

Table : 10 - Hematological parameters at 2 months of life

Parameters	Delayed group (n=49)	Milking group (n=47)	P value	Mean Difference	95% CI
Hematocrit	37.2(±4.5)	36.7(±4.6)	0.662	0.4	-1.6 to 2.4
S.Ferritin	264.3(±86.1)	262.7(±90.1)	0.932	1.6	-36.8 to 40.1

Mean (SD)

At two months of age, there were no significant differences in mean hematocrit and Serum ferritin level between the two groups. The 95% confidence interval (CI) for Serum ferritin level was -36.8 µgm/L to 40.1 µgm/L. The 95% CI for hematocrit was -1.6 to 2.4% .

Table : 11 - Breast feeding and iron supplementation till 2 months of age.

	Delayed clamping (n=42)	Milking (n=41)	P value
Exclusive breast feeding *	36 (85.7)	36 (87.8)	1.000
Iron supplementation *	0	0	

*No. (%)

85.7% in Delayed clamping group and 87.8% in milking group exclusively breastfed their babies. None of the babies received iron as per protocol (Table 11).

Table : 12 - Morbidities between the two groups

	Delayed clamping (n=42)	**Milking (n=41)**
Need for transfusion*	0	0
Post discharge hospitalisation*	0	0

None of the neonates got re-hospitalized during the follow up period of 2 months. Blood transfusion was not given for anemia to any of the neonate during follow up period (Table 12).

Discussion

DISCUSSION

Our study has showed that, milking the extra amount of placental blood, achieved haemoglobin level within the non inferiority margin of 1 gm/dl when compared to delayed cord clamping at 2 minutes in late preterm and term infants which implies that milking is non inferior to delayed cord clamping in achieving the haemoglobin level.

In a study by Gupta and Ramji in 2002, haemoglobin at 3 months of life was significantly higher in delayed cord clamping group (9.9gm/dl) when compared to immediate cord clamping group (8.8gm/dl).

In 2013 Amit Upadhyay et al had showed that mean hemoglobin at 6 weeks was higher in the milking group (11.9 gm/dl) compared to immediate cord clamping group (10.8gm/dl).

In our study, neonates allocated to milking group (12.4 gm/dl) had similar haemoglobin values at 2 months compared with delayed clamping group (12.7 gm/dl), indicating a similar amount of placental blood transfer in both groups. This is relationship might indicate that the procedure of milking four times guarantees the transfer of same amount of placental blood into the neonate when compared to delayed clamping.

An accurate measure of placental transfusion is measuring the circulating blood volume and red cell mass. It would have been preferable

to use the precise measure of placental transfusion rather than measuring the haemoglobin and hematocrit after birth. However, the available method of biotin labelling of red blood cells is time-consuming and difficult to perform on a large number of neonates.

Hosono et al 2008 showed that hemoglobin value at birth in extreme preterm was significantly higher in the milking group (16.5 gm/l) when compared to immediate clamping group (14.1 gm/dl).

In a study by Cernadas et al 2006, the immediate cord clamping group showed significantly lower infant haemoglobin level (17.8 gm/dl) at 24 hours after birth than the delayed clamping group (19.4gm/dl) with mean difference -1.34 g/ dl.

In 2013, Amit Upadhyay et al had showed that at 48 hours of age milking group (11.9gm/dl) had higher haemoglobin level when compared to immediate clamping group (10.8 gm/dl).

Both groups in our study achieved higher mean haemoglobin values at 48 hours (Delayed clamping - 18.4 gm/dl; Milking - 18.9 gm/dl). At 48 hours, Amit Upadhyay et al (10) showed a haemoglobin level of only 11.9gm/dl in the milking group. It was probably because of different method of milking used by them. In our study, milking the umbilical cord was done towards the baby with an intact cord and no clamping was done. The baby had better chance of getting larger

placental transfusion when compared with them where baby received only the blood remaining in 20 cms of cut cord and there was no connectivity with the placenta (Umbilical cord was cut from the placenta and then milked towards the baby). Intactness of the umbilical cord with the placenta till the end of milking adopted in our study, 100% of antenatal iron supplementation and lesser percentage of maternal anemia in our study would have been the reasons for higher mean haemoglobin value in our study.

Our results show that milking the cord four times may be adequate and produced comparable haemoglobin levels both at 48 hrs and at 2 months with two minutes of delayed cord clamping. The inclusion of another control group of neonates randomized to immediate cord clamping would have been useful but was felt superfluous because already several studies had established the beneficial effects of delayed cord clamping.

Rabe et al placed the newborns 20 cm below the level of mother, which could lead to a gravity-dependent flow of blood from mother to baby. To avoid this, we kept the neonates at the level of uterus in both the groups.

Our results are somewhat similar to a recent trial by Rabe et al (45) which showed that milking the umbilical cord 4 times in very low birth

weight babies led to similar amount of placento-fetal blood transfusion compared with delayed cord clamping.

We adopted the same milking technique used by Rabe et al (45). Amit Upadhayay et al also used the same speed 10cm/sec for umbilical cord milking but they milked it three times only. However, Amit Upadhyay et al and Tarnow- Mordi et al did the milking after clamping and cutting the umbilical cord.

With regarding to need for phototherapy, five trials (1762 infants) (Emhamed 2004; McDonald 1996; Nelson 1980; Oxford Midwives 1991; van Rheenen 2007) had showed significantly fewer infants in the immediate cord clamping group requiring phototherapy for jaundice than in the delayed cord clamping group (RR 0.59, 95% CI 0.38 to 0.92). This equates to 3% of infants in the early clamping group and 5% in the late clamping group, a risk difference of 2% (95% CI -0.04 to 0.00).

In our study about 10% of neonates in each group had significant hyperbilirubinemia requiring phototherapy which was higher than those found in previous studies and in study by Amit upadhayay et al, in which none of the neonates had significant hyperbilirubinemia requiring phototherapy.

No polycythemia was recorded in both the groups in our study. These results are similar to Amit Upadhayay et al study in which none of

the neonates had polycythemia. Three other trials **(**Cernadas 2006; Emhamed 2004; Van Rheenen 2007) also showed that there was no difference in polycythemia between the immediate and delayed cord clamping groups.

In one trial of 107 infants (Geethanath 1997), infant ferritin levels were significantly higher in the delayed clamping group (73.6 µg/L) compared with immediate clamping group (55.7µg/L) with mean difference of 17.90 µg/L at three months.

At four months, Andersson et al showed a 45% improvement in serum ferritin level between the delayed clamping group and immediate cord clamping group (Ferritin level in delayed clamping group-117µg/L and immediate cord clamping group - 81µg/L)

A*t* six months, Ferritin levels were significantly higher in the late clamping group compared with early clamping (mean difference of 11.80 ug/L, Chaparro 2006).

Serum ferritin at 6 weeks was significantly higher in milking group (355.9µg/L) than in immediate clamping group (177.5 µg/L) (Amit Upadhayay et al 2013)

Our study had showed that at two months, there were comparable levels of serum ferritin between the delayed cord clamping group

(264.3µg/L) and milking group (262.7µg/L) with mean difference of 1.6 µg/L.

Serum ferritin level achieved at 6 weeks in the milking group of Amit Upadhayay et al 2013 was higher when compared to our milking group (value 355.9 µg/L versus 262.7 µg/L). Though our serum ferritin value was less when compared to this study but definitely much higher than the immediately clamping group of Amit Upadhayay et al.

Regarding neonates admitted for respiratory distress, our study had reported relatively higher percentage (6.3% in delayed clamping group and 4.1% in milking group) when compared to Amit upadhayay et al, in which none of the neonates were hospitalised for respiratory distress at birth. This was probably because of more placental blood transfused to the neonates in our cohort as demonstrated by higher haemoglobin value at 48 hours.

The strengths of our study were:

- The main strength of our study is that it is a randomized control trial with appropriate sample size.
- The technique of umbilical cord milking was standardized by meticulous demonstrations to all doctors on duty.
- We used serum ferritin as a measure of iron status.

- In our study all the clinically important side effects of increased placental transfusion have been reported.

The limitations of our study were:

- We did not measure circulating blood volume because it was not feasible in our set up. The available method was beyond the scope of our infrastructure.
- We measured the serum bilirubin level only at 48 hours to avoid frequent blood samplings.
- Since the randomisation was done before delivery, post randomisation exclusion was unavoidable but it was only a minor percentage. (5.7% in delayed clamping group and 7.8% in milking group)
- Our follow-up duration was relatively short.

Conclusion

CONCLUSION

1. Umbilical cord milking is as effective as delaying the umbilical cord clamping in achieving higher haemoglobin levels at two months of age in late preterm and term infants delivered both by caesarean section and vaginal route.

2. Umbilical cord milking and delayed cord clamping resulted in comparable levels of haemoglobin and hematocrit at 48 hours of life implying that similar amount of placental transfusion occurs in both the groups.

3. Milking the umbilical cord resulted in similar iron stores when compared to that of the delayed cord clamping.

4. Umbilical cord milking does not produce significant hemodynamic disturbances.

5. Frequency of adverse effects like significant hyperbilirubinemia requiring phototherapy, respiratory distress and Polycythemia were similar in both the groups.

Implication for practice

Umbilical cord milking may be safely instituted in situations where delayed umbilical cord clamping is practically difficult to perform delayed cord clamping in late preterm and term infants.

Implication for further research

1. Further studies with longer follow-up till 6-12 months are desirable to establish whether the initial advantage in haemoglobin and ferritin is sustained later in infancy.
2. Further larger studies with neurodevelopment as an outcome may be considered.

Bibliography

BIBLIOGRAPHY

1. Yao AC, Lind J. Blood flow in the umbilical vessels during the third stage of labour. *Biology of the Neonate*. 1974;25:186-193.

2. Dewey KG, Chaparro CM. Session 4: Mineral metabolism and body composition iron status of breast-fed infants. *The Proceedings of the Nutrition Society*. 2007;66(3):412-422.

3. Duley LMM, Weeks AD, Hey EN, Drife JO. Clamping of the umbilical cord and placental transfusion. Royal College of Obstetricians and Gynaecologists. 2009.

4. Prendiville WJP, Elbourne D, McDonald SJ. *Active versus expectant management in the third stage of labour* [Cochrane review]. Chichester: The Cochrane Library; 2000.

5. *Management of the third stage of labour to prevent post-partum haemorrhage (joint statement)*. The Hague and London: International Confederation of Midwives and International Federation of Gynaecology and Obstetrics; 2003.

6. Van Rheenen PF, Brabin BJ. A practical approach to timing cord clamping in resource poor settings. *BMJ* 2006; 333: 954-8 doi:10.1136/bmj.39002.389236.BE pmid: 17082547.

7. BeardJ.Recent evidence from human and animal studies regarding iron status and infant development. J Nutr2007;137:524-30S.

8. Carlson ES, TkacI, MagidR, O'Connor MB ,Andrews NC, Schallert T, et al. Iron is essential for neuron development and memory function in mouse hippocampus. J Nutr 2009;139:672-9.

9. Mathew JL. Timing of umbilical cord clamping in term and preterm deliveries and infant and maternal outcomes: a systematic review of randomized controlled trials. Indian Pediatr 2011.

10. Amit Upadhayay et al. American journal of Obst. & Gynac. february 2013.

11. Bradley J, Leibold E A, Harris Z L, Wobken J D, Clarke S, Zumbrennen K B *et al.* Influence of gestational age and fetal iron status on IRP activity and iron transporter protein expression in third-trimester human placenta. *American Journal of Physiology Regulatory, Integrative and Comparative Physiology*. 2004; 287(4):R894-R901.

12. Brown MS. Physiologic anemia of infancy: Normal red-cell values and physiology of neonatal erythropoiesis. In: JA Stockman III, (ed). Developmental and Neonatal Hematology. New York: Raven Press. 1988. pages 249-273.

13. Domellof MD, Cohen RJ, Dewey KG, Hernell O, Rivera LL, Lonnerdal B. Iron supplementation of breast-fed Honduran and Swedish infants from 4 to 9 months of age. *Journal of Pediatrics*. 2001;138(5):679-687.

14. Dallman PR, Yip R, Oski FA. Iron deficiency and related nutritional anemias. In: Orkin S, Nathan D, Ginsburg D, Look A, Fisher D, Lux S, (eds). Hematology of Infancy and Childhood. Philadelphia: W.B. Saunders and Company. 1993.

15. Chaparro C M. Setting the stage for child health and development: prevention of iron deficiency in early infancy. *Journal of Nutrition*. 2008;138(12):2529-2533.

16. Oski F A, Landaw S A. Inhibition of iron absorption from human milk by baby food. *American Journal of Diseases of Children*. 1980;134(5):459-460.

17. Lozoff B, Beard J, Connor J, Barbara F, Georgieff M, Schallert T. Long-lasting neural and behavioral effects of iron deficiency in infancy. *Nutritional Review*. 2006;64:S34-S43.

18. Rao R, Tkac I, Townsend EL, Ennis K, Gruetter R, Georgieff MK. Perinatal iron deficiency predisposes the developing rat hippocampus to greater injury from milk to moderate hypoxia-ischemia. *Journal of Cerebral Blood Flow Metabolism*. 2007;27(4):729-740.

19. Ward KL, Tkac I, Jing Y, Felt B, Beard J, Connor J *et al.* Gestational and lactational iron deficiency alters the developing striatal metabolome and associated behaviors in young rats. *Journal of Nutrition.* 2007;137:1043-1049.

20. Rao R, Tkac I, Townsend EL, Gruetter R, Georgieff MK. Perinatal iron deficiency alters the neurochemical profile of the developing rat hippocampus. *Journal of Nutrition*. 2003;133:3215-3221.

21. De Pee S, Bloem MW, Sari M, Kiess L, Yip R, Kosen S. The high prevalence of low hemoglobin concentration among Indonesian infants aged 3-5 months is related to maternal anemia. *Journal of Nutrition*. 2002;132:2215-2221.

22. Kilbride J, Baker TG, Parapia LA, Khoury SA, Shuqaidef SW, Jerwood D. Anaemia during pregnancy as a risk factor for iron-

deficiency anemia in infancy: a case-control study in Jordan. *International Journal of Epidemiology*. 1999;28:461-468.

23. Preziosi P, Prual A, Galan P, Daouda H, Boureima H, Hercberg S. Effect of iron supplementation on the iron status of pregnant women: consequences for newborns. *American Journal of Clinical Nutrition*. 1997;66:1178-1182.

24. Colomer J, Colomer C, Gutierrez D, Jubert A, Nolasco A, Donat J *et al.* Anaemia during pregnancy as a risk factor for infant iron deficiency: Report from the Valencia Infant Anaemia Cohort (VIAC) study. *Paediatric and Perinatal Epidemiology*. 1990;4(2):196-204.

25. Stoltzfus R J. Research needed to strengthen science and programs for the control of iron deficiency and its consequences in young children. *Journal of Nutrition*. 2008;138(12):2542-2546.

26. Duley LMM, Weeks AD, Hey EN, Drife JO. Clamping of the umbilical cord and placental transfusion. Royal College of Obstetricians and Gynaecologists. 2009.

27. Enkin M, Keirse M, Neilson J, Crowther C, Duley L, Hodnett E *et al.* A guide to effective care in pregnancy and childbirth. 3rd ed. Oxford: Oxford University Press. 2000.

28. Farrar D, Airey R, Law GR, Tuffnell D, Cattle B, Duley L. Measuring placental transfusion for term births: weighing babies with cord intact. BJOG 2011;118:70–5.

29. Narendra AB, Beckett C, Aitchison T, Kyle E, Coutts J, Turner T, et al. Is it possible to promote placental transfusion (PTFx) at preterm delivery? Abstract 213. Pediatr Res 1998;44:454.

30. Brune T, Garritsen H, Witteler R, Schlake A, Wu¨llenweber J, Louwen F, et al. Autologous placental blood transfusion for the therapy of anaemic neonates. Bio Neonate 2002.

31. Yao ac, moinian m, distribution of blood between infant and placenta after birth. Lancet 1969.

32. Dewey KG, Chaparro CM, mineral metabolism and body composition. P Nutri soc 2007.

33. Andersson O, Hellstrom Westas L, AnderssonD, Domellof M. Effect of delayed versus early umbilical cord clamping on neonatal outcomes and iron status at 4 months :a randomized controlled trial. BMJ.2011.

34. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. J McDonald, Philippa Middleton et al. Cochrane review 2008.

35. Hutton EK, Hassan ES. Late vs early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. JAMA 2007.

36. Rabe H, Reynolds G, Diaz-Rossello J. Early versus delayed umbilical cord clamping in preterm infants. Cochrane Database Syst Rev 2004;(4):CD003248.

37. Rabe H, Reynolds G, Diaz-Rossello J. A systematic review and metaanalysis of a brief delay in clamping the umbilical cord of preterm infants. Neonatology 2008;93:138–44.

38. Mercer JS, Vohr BR, McGrath MM, Padbury JF, Wallach M, Oh W. Delayed cord clamping in very preterm infants reduces the incidence of intraventricular hemorrhage and late-onset sepsis: a randomized, controlled trial. Pediatrics 2006;117:1235–4.

39. Winter C, Macfarlane A, Deneux-Tharaux C, Zhang WH, Alexander S, Brocklehurst P *et al.* Variations in policies for management of the third stage of labour and the immediate management of postpartum haemorrhage in Europe. *British Journal of Obstetrics and Gynaecology*. 2007;114(7):845-854.

40. Mercer JS, Nelson CC, Skovgaard RL. Umbilical cord clamping: beliefs and practices of American nurse-midwives. *Journal of Midwifery & Women's Health*. 2000;45(1):58-66.

41. Ononeze et al. Attitude of obstetritian towards DCC. Questionnaire based study Ononeze et al, J. obstet. Gynac 2009.

42. Hosono S, Mugishima H, Fujita H, et al. Blood pressure and urine output during the first 120 hours of life in infants born at less than 29 weeks gestation related to umbilical cord milking. Arch Dis Child fetal and neonatal ed. 2009; 94:F328–31. [PubMed: 19221402].

43. Hosono S, Mugishima H, Fujita H, et al. Umbilical cord milking reduces the need for red cell transfusions and improves neonatal

adaptation in infants born at less than 29 weeks gestation: a randomized controlled trial. Arch Dis Child Fetal neonatal ed. 2008.

44. Erickson, Owen, Mercer et al. Umbilicalcord milking in term infants delivered by cesarean section. J perinatology November 2011.

45. Rabe et al. Milking Compared With Delayed Cord Clamping to Increase Placental Transfusion in Preterm Neonates - A Randomized Controlled Trial. Obstetri Gynac feburary 2011.

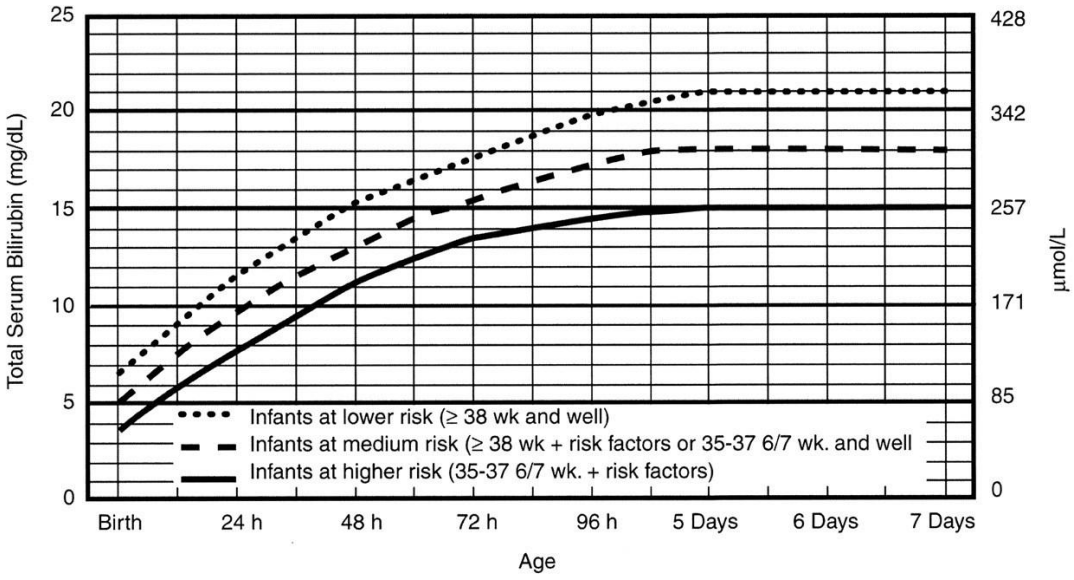
Annexures

ANNEXURE - 1

Parameters	0	1	2
RR Per min.	<60	60-80	>80
Cyanosis	Absent	In room air	In 40% oxygen
Grunt	Absent	Audiable with stethscope	Audible with naked ear
Retraction	Absent	Mild	Moderate-severe
Air entry	Good	Diminished	Barely audible

DOWNES score

ANNEXURE -2



AAP nomogram for phototherapy

ANNEXURE – 3

PARENT DATA COLLECTION FORM

Mother's name	:	Father's name	:
Age	:	Age	:
Educational status	:	Educational status	:
Job	:	Job	:
Income	:	Income	:
Address	:	Phone no.	:

Home Distance in km	:
Mother blood group and typing	:
No. of antenatal visits	:
Prepregnant weight	:
Present weight	:
Weight gain	:
Intervention group	: Delayed clamping / Milking
LMP	:
EDD	:
Scan EDD [first trimester]	:
Gestation age	:
Antenatal iron supplementation	:
Hemoglobin %	:
Use of oxytocin	: Yes / No
Socioeconomic status (Modified kuppusamy scale)	: 1 / 2 / 3 / 4 / 5

ANNEXURE – 4

NEONATAL DATA COLLECTION FORM

Name : DOB:

Sex : TOB:

Disc no. :

Birth weight in grams :

Gestation age :

Mode of delivery : Vaginal / LSCS

Intervention group : DCC / UCM

Hemodynamic parameters

Parameters	At 30 minutes	48 hours
Heart rate		
Respiratory rate		

Clinical parameters

Parameter	At birth	Till discharge
Respiratory distress		
Jaundice requiring phototherapy		Yes/No. if yes duration of phototherapy.....

Hematological parameters

Parameters	48 hours	2 months
Hemoglobin		
Hematocrit		
S. Bilirubin		
S. Ferritin		

Peak bilirubin level :

Breast Feeding at 2 months : Exclusive breast feeding / Partial.

Post discharge hospitalisation :

ANNEXURE - 5

INFORMATION SHEET

Title : **"Comparison of Delayed cord clamping versus Umbilical cord milking in late preterm and term infants"-An open label randomised controlled trial.**

Participant name : ..... Serial no:.....

Investigator name:..... Date : .....

• In our country, iron deficiency anemia is a common problem in young children. There are many ways to prevent iron deficiency anemia, one among them is to increase the transfer of amount of blood and its iron content to newborn baby from the mother immediately following delivery.

There are two different methods by which this enhanced transfer of blood and its iron content to the baby can be achieved namely delayed clamping of umbilical cord and umbilical cord milking and then early clamping.

Current evidences shows that both methods individually improve the transfer of placental blood to the new born baby. At present there are no scientific studies comparing the above two methods.

Our present study is to compare the effect of the two methods of umbilical cord clamping on hemoglobin levels, iron storage level (serum ferritin) .We are conducting this study in well babies born through either vaginal route or caesarean section at Institute of Obstetrics and Gynecology and Hospital for women and children, Egmore, Chennai.

If you are found eligible, we will allocate your baby randomly to receive any of the interventions. Baby's general condition will be monitored and at 48 hours venous blood (one ml) for hemoglobin, hematocrit and serum bilirubin will be obtained and again at 2 months venous blood (one ml) sample for hemoglobin, and serum ferritin will be obtained from your baby. This study will not in any way affect your management or management of your baby.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled. The results of the study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

.....	.....	.....
Participant name	Signature	Date
.....	.....	.....
Investigator name	Signature	Date

ANNEXURE - 6

CONSENT FORM

Title : **"Comparison of Delayed cord clamping versus Umbilical cord milking in late preterm and term infants"-An open label randomized controlled trial.**

Participant name : ..... Serial no:.....
Investigator name:..... Date : .....

I Mrs/Mr._____ M/O, F/O,B/O _____
Sex_____ Hosp. No._____ admitted in the Institute of Obstetrics and Gynecology and Hospital for Women and Children, Egmore, Chennai was explained by the doctor about the two different methods of umbilical cord clamping at the time of delivery of my baby.

I am willing for my baby to be enrolled in the delayed cord clamping versus Umbilical cord milking trial. The doctors have explained to me the nature and the purpose of the trial. I have given my consent only after completely understanding the details that were explained to me.

I am willing for my baby to be enrolled in this study without any ones compulsion and I am fully aware that I can withdraw from the trial at any time during the study.

I have given consent for administering either delayed cord clamping or milking of the umbilical cord at the time of delivery as per the study protocol. I have also given my consent for drawing one ml of blood at 48 hours of life and again at 2 months of life by venipuncture for laboratory investigations during the study.

The adverse effects (respiratory distress, polycythemia, Jaundice) were explained to me. I have given this consent to be enrolled in this study with my full consciousness.

.....	.....	.....
Participant name	Signature	Date
.....	.....	.....
Investigator name	Signature	Date

ANNEXURE – 7

ஆராய்ச்சி தகவல் தாள்

ஆய்வு தலைப்பு:

நிறைமாத மற்றும் பிந்தி குறைமாத குழந்தைகளுக்கான காலம் தாழ்த்தி தொப்புள் கொடியை துண்டாக்குதல் அல்லது தொப்புள் கொடியை கநந்த பின் துண்டாக்குதல் ஆகியவற்றை ஒப்பிடுதல் - பரிசோதனை

பங்குகொள்பவர் பெயர் : தேதி

எண் :

ஆராய்ச்சியாளர் பெயர் :

நம் நாட்டில் இளம் குழந்தைகளுக்கான இரத்தசோகை உள்ளாவதற்கு இரும்பு சத்துக்குறைவே பெரும்பான்மையான காரணமாக உள்ளது.

இந்நோயை தடுப்பதற்கு பல்வேறு வழிகள் உண்டு. குழந்தை பிறக்கும்போது, தாயிடமிருந்து சேய்க்கு செல்லும் இரத்தத்தையும் இரும்பு சத்தையும், (தொப்புள் கொடி மூலம்) அதிகரிப்பதும் அவற்றுள் ஒன்று.

இதனை இருவேறு வழிகளில் செயல்படுத்தவும், முதல்வகை தொப்புள் கொடியை துண்டிக்கும் காலத்தை நீட்டிப்பதன் மூலமாகவும், மற்றொரு வகையில் தொப்புள் கொடியில் தங்கும் இரத்தத்தை முழுவதுமாய் கறந்து பின்பு தொப்புள் கொடியை துண்டித்து பிணைப்பதன் மூலமாகவும் செயல்படுத்தலாம்.

சமீபத்திய ஆதாரங்களின்படி, சேய்க்கு தாயிடமிருந்து கிடைக்கும் இரத்தம் மற்றும் இரும்புசத்து மேற்கூறிய இருவேறு முறைகளினாலும் கிடைக்கும் என்பது உறுதிப்படுத்தப்பட்டுள்ளது.

நாங்கள் மேற்கொள்ளப்போகும் இந்த ஆய்வின் நோக்கம், மேற்சொன்ன இருவேறு முறைகளினாலும் குழந்தைகளினாலும் குழந்தைகளின் ஹீமோகுளோபின் மற்றும் இரும்புச்சத்து சேமிப்பின் அளவில் ஏற்படும் மாற்றங்களை ஒப்பிடுவதே ஆகும்.

இந்த ஆய்வை, மகப்பேறு மற்றும் பெண்கள் நோயியல் மையம் மற்றும் குழந்தைகள் மருத்துவமனை மற்றும் ஆராய்ச்சி மையத்தில் சுகபிரசவம் மற்றும் அறுவை சிகிச்சை மூலம் பிறக்கும் ஆரோக்கியமான குழந்தைகளுக்கு நடத்த உள்ளோம்.

உங்கள் குழந்தை இந்த ஆய்விற்கு தகுதியுள்ளதாக இருப்பின், குழந்தை, மேற்கூறிய இருமுறைகளிலும் ஏதேனும் ஒன்றிற்கு வகைப்படுத்தப்படும்.

குழந்தைகளின் உடல்நிலை கண்காணிக்கப்படுவதோடு 48 மணிநேரம் கழித்து இரத்தநிறமி (ஹீமோகுளோபின்) பித்தநிறமி (டைசைரடின்) போன்றவற்றின் அளவை அறிய குழந்தையிடமிருந்து 1மில்லி இரத்தம் பெறப்படும் இரத்தப்பரிசோதனையும் மேற்கொள்ளப்படும். பின் இரண்டு மாதம் கழித்து இதில் ஏற்படும் மாறுபாட்டை அறிய இரத்தநிறமி (ஹீமோகுளோபின்) இரும்பு சத்து சேமிப்பின் அளவு போன்றவற்றிற்கான மீண்டும் 1 மில்லி இரத்தம் எடுக்கப்பட்டு பரிசோதனைகளும் மேற்கொள்ளப்படும்.

இந்த ஆய்வினால் குழந்தையின் மருத்துவ சிகிச்சையில் எவ்வித மாறுபாடும் ஏற்படாது. இந்த ஆய்வு குறித்த எல்லா விவரங்களும் ரகசியமாக பாதுகாக்கப்படும் தனிப்பட்ட நபர் குறித்து எந்த விபரங்களும் வெளியிடப்படமாட்டாது.

இந்த ஆய்வில் பங்கு கொள்வது அவரவர் விருப்பம் சார்ந்தது. நீங்கள் இந்த ஆய்விலிருந்து விலக நினைக்கும் பட்சத்தில் தாராளமாக விலகலாம். உங்களின் இந்த முடிவானது குழந்தையின் மருத்துவ சிகிச்சையில் எவ்வித பாதிப்பையும் ஏற்படுத்தாது என்று உறுதி கூறுகிறேன்.

இந்த ஆய்வின் முடிவு தங்களுக்கு ஆய்வின் இறுதியில் தெரிவிக்கப்படும் அல்லது ஆய்வு நிகழும்போதே ஏதெனும் மாறுபாடு இருந்தால் குழந்தையின் சிகிச்சைக்கு உதவும் பொருட்டு அம்முடிவு உடனடியாகத் தெரிவிக்கப்படும்.

பங்கு கொள்வோர் பெயர்	கையொப்பம்	தேதி
ஆராச்சியாளர் பெயர்	கையொப்பம்	தேதி

ANNEXURE - 8

ஒப்புதல் படிவம்

ஆய்வு தலைப்பு:

நிறைமாத மற்றும் பிந்தி குறைமாத குழந்தைகளுக்கான காலம் தாழ்த்தி தொப்புள் கொடியை துண்டாக்குதல் அல்லது தொப்புள் கொடியை கறந்த பின் துண்டாக்குதல் ஆகியவற்றை ஒப்பிடுதல் - பரிசோதனை

பங்குகொள்பவர் பெயர் : தேதி

எண் :

ஆராய்ச்சியாளர் பெயர் :

நான் திரு.திருமதி ..... தபெ (அ) த.பெ, (அ) க.பெ ..... பாலினம் ..... மருத்துவமனை எண். ..... கீழ் அரசு மகப்பேறு பெண்கள் நோயியல் மற்றும் அரசு குழந்தைகள் மருத்துவமனையில் (மகப்பேறு சிகிச்சைக்காக) பிரசவத்திற்காக அனுமதிக்கப்பட்டு உள்ளேன். மருத்துவர் வாயிலாக, குழந்தை பிரசவிக்கும் தருணத்தில், இருவேறு முறைகளால் தொப்புள் கொடி மூலம் இரத்தம் மற்றும் இரும்புச்சத்து பரிமாற்றத்தை தாயிடமிருந்து சேய்க்கு அஃதிகரிப்பது குறித்து எனக்கு விளக்கப்பட்டது.

நான் எனது குழந்தையை இந்த ஆய்விற்கு உட்படுத்த முழுமனத்துடன் சம்மதிக்கிறேன். எனக்கு இந்த ஆய்வு குறித்த நோக்கமும், ஆய்வைப் பற்றிய விளக்கமும் மருத்துவரால் தெளிவாக விளக்கப்பட்டது. நான் இது குறித்த அனைத்து விபரங்களையும் முழுமையாக புரிந்துணர்வு செய்து கொண்ட பிறகே என் சம்மதத்தை முழுமனத்துடன் தெரிவிக்கிறேன்.

எவ்வித நிர்ப்பந்தமும் இல்லாமல் நான் என் குழந்தையை இந்த ஆய்வில் பங்குபெறச் செய்ய முழுமனதுடன் சம்மதிக்கிறேன். ஆய்வின் எந்தவொரு நிலையிலும், ஆய்விலிருந்து விலகும் முழு உரிமை எனக்கு உண்டு என்பதை நான் நன்கு அறிவேன்.

ஆய்வின் பொருளடக்கத்தின்படி, காலம் தாழ்த்தி தொப்புள் கொடியை துண்டாக்குதல் (அ) தொப்புள் கொடியை கறந்து, விரைவில் துண்டாக்குதல் எனும் இரு வேறு முறைகளில் மேற்கொள்ளப்படும் இந்த ஆய்வில், எந்த இரு வகையிலும் என் குழந்தையை வகைப்படுத்தலாம் எனவும் உறுதி கூறுகிறேன்.

இரத்த பரிசோதனைகளுக்கு, பிறந்த இரண்டாவது நாளிலும் மற்றும் இரண்டாவது மாதத்திலும் சுமார் 1 மில்லி இரத்தம் குழந்தையிடமிருந்து பெறப்படும் என்பதும் எனக்கு மருத்துவர் வாயிலாக தெரிவிக்கப்பட்டது. அதற்கு என் சம்மதத்தை நான் தெரிவித்துக்கொள்கிறேன்.

இச்சிகிச்சையால் விளையும் பாதகங்கள் குறித்தும் எனக்கு விளக்கப்பட்டது.

இந்த ஆய்வில் என் குழந்தை பங்கு பெற என் முழு சம்மதத்தை, சுயநினைவோடு தெரிவித்துக்கொள்கிறேன்.

பங்கு கொள்வோர் பெயர் கையொப்பம் தேதி

ஆராச்சியாளர் பெயர் கையொப்பம் தேதி

Sl. no	R. no.	Name	Sex	Group	Birth weight	Gest. Age	Gestation	Gest. Age	Mode of Delivery	Parity index	Mat Age	Mat. age	Mat. weight	Mat. height	Mat. Hb%	Mat. Hb	Mat. Anemia	Mat. Hb%	Iron supplementation	socioeconomic status	Oxytocin use	Respiratory rate at 30 min	respiratory rate at 48 hours	Heart rate at 30 min	heart rate at 48 hours	Hb% at 48 hrs	Polycythemia	Hct at 48 hrs	S.Bilirubin at 48 hrs	Peak Bilirubin	Hb% at 2 mon	Hct at 2 mon	S.Ferritin at 2 mon	Exclusive breast feeding at 2 months	Admitted for phototherapy	Admitted for Respiratory Distress	Alive or death
1	1	Saradha	1	2	3200	38.4	1	2	2	2	35	2	60	150	2	10.3	1	2	1	2	1	55	44	148	120	18.2	2	54.8	9.6		12.8	37	126.77	1	2	2	1
2	2	Megala	2	2	2850	37.2	1	2	2	2	29	2	66	152	2	9.2	1	2	1	3	1	50	42	140	139	19.7	2	56.8	10.3		11.4	34	277.55	2	2	2	1
3	3	Priya	2	1	3800	38.5	1	2	2	2	25	2	47	151	3	11.5	2	2	1	2	1	43	41	146	158	19.6	2	56	5.3		12	35	264.31	1	2	2	1
4	4	Kavitha	1	2	1440	35.4	2	1	2	2	26	2	70	156	2	10.2	1	2	1	3	1	44	45	155	130	18.2	2	56	8.9		13	39	363.33	1	2	2	1
5	5	Padmavathi	1	2	3200	38.5	1	2	2	2	27	2	81	160	2	10.5	1	2	1	3	1	66	47	154	149	18	2	54	10						2	1	1
6	6	Bhavani	1	2	3000	38.5	1	2	2	2	24	2	85	161	2	9.4	1	2	1	4	1	44	49	148	129	20.5	2	56	15.9	15.9	11.4	34	383.56	1	1	2	1
7	7	Nathiya	1	1	2500	36.6	1	1	2	1	26	2	55	158	2	9.5	1	2	1	2	1	67	51	146	138	20	2	50	9		13	39	328.81	2	2	1	1
8	8	Gunasekari	2	2	2000	36.1	1	1	2	1	36	2	84	159	2	9	1	2	1	3	1	52	52	144	147	18.4	2	51.7	2.2		12.4	36	322.45	1	2	2	1
9	9	Veeraselvi	2	1	3850	39.6	1	2	2	2	22	2	78	154	3	11	2	2	1	3	1	51	54	154	156	15.3	2	45.9	8.4		11.6	33	123.63	2	2	2	1
10	10	Devi	1	1	2750	39.4	1	2	2	2	25	2	56	151	3	12.6	2	2	1	3	1	58	47	158	149	16.6	2	48.9	7.3		10.9	32	253.22	1	2	2	1
11	11	Uma maheshwari	1	2	3440	39.5	1	2	2	1	28	2	65	144	2	9.4	1	2	1	2	1	42	58	152	138	17	2	51.2	7		12	36	267.21	2	2	2	1
12	13	Usharani	1	1	2510	39	1	2	2	2	29	2	54	152	2	10.8	1	2	1	3	1	50	45	150	127	16	2	48.4	3.6		10	28	209.12	1	2	2	1
13	14	Koteeshwari	2	1	2400	39.5	2	2	2	2	29	2	64	144	2	9.4	1	2	1	4	1	51	44	159	129	22.6	2	60.2	16.8	17.2					1	2	1
14	15	Lakshmi	2	1	3315	38.6	1	2	2	2	28	2	70	156	2	10.5	1	2	1	3	1	70	43	145	138	18.9	2	51.5	1.6		13.1	40.2	357.74	1	2	1	1
15	16	Nathiya	2	2	2800	36.3	1	1	1	2	24	2	60	144	2	9.4	1	2	1	4	1	47	40	144	146	17	2	51	1.8						2	2	1
16	17	Devika	2	2	3000	39.5	1	2	1	1	19	2	78	149	2	10.1	1	2	1	4	1	53	42	149	157	14.7	2	44.1	2.1		11	31	388.46	1	2	2	1
17	18	Anushya	2	1	2800	39.4	1	2	1	2	22	2	70	154	2	10.2	1	2	1	2	1	50	43	165	129	18.1	2	53.9	7.3		10.5	30	299.97	1	2	2	1
18	19	Sujatha	1	1	3380	39.1	1	2	1	2	26	2	63	160	2	9.9	1	2	1	3	1	52	41	148	138	18.9	2	52.4	7.8		11.7	32	217.67	1	2	2	1
19	20	Revathi	1	2	3000	42	1	2	1	1	24	2	67	159	2	10.6	1	2	1	3	1	52	48	144	146	17.4	2	52.2	8.2		13	39	271.11	1	2	2	1
20	21	Divya	1	2	2860	40	1	2	1	1	18	1	75	152	2	9.2	1	2	1	3	1	54	53	140	157	17.8	2	52.4	5.6		13.5	40.2	167.73	1	2	2	1
21	22	Adhila parveen	2	2	1660	38.6	2	2	1	1	19	2	45	140	2	10.2	1	2	1	3	1	49	55	135	126	15	2	45	5.2		9.4	27	279.98	2	2	2	1
22	23	Anathi	1	2	2940	39.5	1	2	2	2	28	2	75	153	2	10.2	1	2	1	3	1	48	54	120	138	17	2	46.4	1.5		10.7	30	174.45	1	2	2	1
23	24	Deepa lakshmi	2	1	2170	34.2	1	1	2	2	33	2	50	162	3	12.9	2	2	1	3	1	56	53	134	149	19.2	2	57	17	17	10.1	30	168.56	2	1	2	1
24	25	Kaniyammal	2	2	3090	38	1	2	2	2	36	2	60	152	3	12.5	2	2	1	2	1	54	47	129	159	20.4	2	55	16.7	16.7	12.6	35	205.77	1	1	2	1
25	26	Lakshmi	2	2	3150	40.2	1	2	2	2	25	2	70	150	2	10.2	1	2	1	3	1	51	43	130	129	20.9	2	55	16.7	16.7	14	42	388.52	1	1	2	1
26	27	Barathi	1	1	3200	38.4	1	2	2	2	27	2	75	153	3	11.8	2	2	1	3	1	53	51	150	138	18.7	2	50	12.1		11.7	33	231.11	1	2	2	1
27	28	Gunapusanam	2	2	2820	37.6	1	2	2	2	28	2	71	156	2	10.5	1	2	1	4	1	56	50	135	147	15.8	2	43	10.4		8.9	24	90.89	1	2	2	1
28	29	Devi	2	1	2890	38.6	1	2	2	2	32	2	85	154	2	9.4	1	2	1	2	1	57	50	139	156	18.3	2	52	5		13.8	41.4	302.44	1	2	2	1
29	30	Karthiga	2	1	3850	39	1	2	2	2	21	2	89	166	3	12.8	2	2	1	3	1	47	51	148	159	18.1	2	46	11.9		13.9	41.7	311.23	1	2	2	1
30	31	Anushiya	1	2	3890	37.5	1	2	2	2	25	2	70	155	2	10.5	1	2	1	3	1	49	50	127	148	16.8	2	47	9.4						2	2	1
31	32	Rajathi	1	2	2290	40.1	1	2	2	1	20	2	44	142	3	13.3	2	2	1	3	1	50	52	129	138	20.1	2	55	9.2		11	33	275.62	1	2	2	1
32	33	Sangeetha	1	2	3000	38	1	2	1	2	24	2	70	156	3	11	2	2	1	3	1	53	48	123	127	19.6	2	58.8	15.4		13.2	39.6	304.42	2	2	2	1
33	34	Bhuvaneshwari	2	1	2780	38.3	1	2	2	2	24	2	67	150	2	9.4	1	2	1	4	1	42	50	139	138	18	2	51	7.4		12	35	205.56	1	2	2	1
34	35	Sarmila	2	1	3200	39.4	1	2	2	2	33	2	71	160	3	11.5	2	2	1	3	1	48	51	148	128	19.2	2	57.8	4.2		14.6	41.7	378.61	1	2	2	1
35	36	Thulasi	1	1	2540	39.2	1	2	2	2	29	2	70	150	2	10.5	1	2	1	2	1	69	53	146	140	15	2	42	8.3		11	31.4	79.56	2	2	1	1
36	37	Bhanumathi	1	2	2950	39.2	1	2	2	1	25	2	49	146	2	10.5	1	2	1	2	1	50	55	155	123	15.6	2	42	4.9		9.1	29	352.51	1	2	2	1
37	38	Jenifar	2	2	2450	36.2	1	1	1	1	23	2	65	153	2	10.2	1	2	1	3	1	53	56	140	148	19.3	2	53	5.5		12.1	32.3	405.56	1	2	2	1
38	39	Kanagi	2	1	3800	41.3	1	2	1	2	26	2	68	156	3	12.2	2	2	1	3	1	54	46	150	159	18.6	2	56	9		12	33.5	388.67	1	2	2	1
39	40	sarala	2	1	2465	38	2	2	1	1	24	2	49	156	2	9	1	2	1	3	1	56	49	152	129	21.6	2	57	16.7	16.7	14.6	41.7	205.57	1	1	2	1
40	41	Glory	2	2	3750	40.3	1	2	2	2	24	2	55	155	2	9.6	1	2	1	3	1	51	48	158	150	22.3	2	60	16.1	16.1	13.3	38	187.67	1	1	2	1
41	42	Vijayalakshmi	2	2	3295	39.2	1	2	2	2	30	2	90	151	3	11.5	2	2	1	4	1	52	50	155	155	18.1	2	55	14.6		13.5	40.5	206.55	1	2	2	1
42	43	Roshini	2	1	2965	38.5	1	2	1	2	20	2	50	145	1	8.9	1	1	1	2	1	54	51	159	144	18.9	2	52	6.7		11	33	178.89	1	2	2	1
43	44	Bobby	1	1	2550	36.1	1	1	2	1	24	2	70	165	3	11.1	2	2	1	3	1	50	54	149	159	19.5	2	53	8.5						2	2	1
44	45	Kalpana	1	1	3650	40	1	2	1	1	24	2	75	160	2	9.2	1	2	1	3	1	48	53	146	134	19.7	2	55	9.1		14.6	41.7	177.14	1	2	2	1
45	47	Kalaiarasi	2	1	3250	35.3	1	1	1	1	19	2	67	154	2	9.4	1	2	1	3	1	50	50	142	143	18.9	2	52	12.1		12.5	36	234.62	1	2	2	1
46	49	Preethi	2	1	2940	39	1	2	1	1	21	2	61	153	2	9.5	1	2	1	3	1	52	51	149	123	18.6	2	56	13.2		12.5	36	207.56	1	2	2	1
47	50	Sandhiya	2	1	3500	40.6	1	2	2	1	20	2	69	158	2	10.4	1	2	1	4	1	51	49	139	132	19.9	2	56	10.6						2	2	1

48	51	Vidhiya	1	2	3130	40.4	1	2	1	2	23	2	49	162	1	8.9	1	1	1	4	1	49	48	158	143	18.6	2	55.8	5.6						2	2	1
49	52	Prameela	2	2	3550	40.4	1	2	1	1	21	2	65	147	2	9.1	1	2	1	2	1	52	50	137	134	17.9	2	53.7	7.2		14	42	78.57	1	2	2	1
50	53	Rajalakshmi	1	1	2890	40.1	1	2	1	2	23	2	55	150	2	10.1	1	2	1	2	1	53	51	156	145	17.5	2	52.5	5.1		13	39	207.37	1	2	2	1
51	54	Maheswari	1	2	2860	37.1	1	2	1	1	35	2	92	152	3	11.5	2	2	1	3	1	66	54	153	154	20.7	2	56	15.2		13.8	39	211.12	1	2	1	1
52	55	Uma	2	2	2400	40.1	2	2	1	2	24	2	56	148	2	9.4	1	2	1	3	1	49	51	159	156	17.3	2	53.8	6		12.5	37.5	201.12	1	2	2	1
53	56	Deepa	2	2	2500	36.4	1	1	1	1	23	2	69	159	2	10.9	1	2	1	3	1	50	50	160	147	18.9	2	54	9.6						2	2	1
54	59	Luthiya	1	1	2745	40.4	1	2	1	1	20	2	56	160	2	10.3	1	2	1	3	1	54	48	151	138	17.3	2	53.8	11.6		12.5	37.5	367.87	1	2	2	1
55	60	Kovindammal	1	2	3275	38.1	1	2	2	2	27	2	67	165	2	10.5	1	2	1	3	1	55	49	149	129	15.2	2	45.6	2.7		9.7	28	257.62	2	2	2	1
56	61	Rekha	1	1	2780	39.4	1	2	2	2	24	2	53	143	2	9.2	1	2	1	3	1	56	51	136	126	18	2	48	11.4		11	30	389.67	1	2	2	1
57	63	Priya	2	2	3100	38.2	1	2	2	2	23	2	65	154	2	10.5	1	2	1	3	1	52	53	139	137	16.5	2	48	12.6		12.5	37.2	355.67	1	2	2	1
58	64	Sangeetha	1	2	3370	38.2	1	2	2	2	24	2	60	152	2	9.8	1	2	1	3	1	54	54	142	148	17.3	2	53.8	13.1		13.8	39	307.85	1	2	2	1
59	65	Jasimin	2	2	3440	40.1	1	2	2	1	27	2	60	140	2	9.2	1	2	1	3	1	50	55	149	159	14.8	2	40	12.6		11	33	190.98	1	2	2	1
60	66	Kanchana	1	2	3100	40	1	2	2	1	28	2	69	159	2	10.9	1	2	1	3	1	52	45	129	160	17.3	2	54	8.9		13.8	39	137.89	1	2	2	1
61	67	Indhu	2	1	3180	39.9	1	2	1	1	22	2	84	161	2	10.5	1	2	1	3	1	51	47	140	120	16.5	2	48	9.1		12.4	37	172.23	1	2	2	1
62	69	Sasikala	1	1	3600	38.5	1	2	2	2	26	2	64	155	2	9	1	2	1	4	1	49	40	149	139	17	2	44	5.2		13.8	39.1	291.67	2	2	2	1
63	70	Revathi	1	1	2630	38.1	1	2	2	2	26	2	60	148	2	9.8	1	2	1	2	1	53	42	158	148	17.3	2	54	7.2		12	36.3	287.56	1	2	2	1
64	71	Parameshwari	2	1	2730	38.5	1	2	2	2	25	2	71	156	2	9.5	1	2	1	3	1	55	43	150	157	17.1	2	51.3	6.2						2	2	1
65	72	Anjali	2	2	3230	39.3	1	2	2	2	23	2	70	162	3	12.5	2	2	1	2	1	56	49	147	126	18.1	2	54.6	7.2		12.5	36.5	352.45	1	2	2	1
66	73	Bhavani	2	1	2500	39.4	2	2	2	1	24	2	44	142	2	10.8	1	2	1	3	1	52	47	139	137	16.5	2	49.5	7.7		12.2	36.6	222.85	1	2	2	1
67	74	Shalini	2	1	3000	41	1	2	2	1	28	2	74	155	2	10.3	1	2	1	3	1	53	51	129	148	16.8	2	50.4	4.3		12.4	37.4	299.45	1	2	2	1
68	75	Jayalakshmi	2	2	3375	39.4	1	2	2	2	29	2	75	147	2	10	1	2	1	3	1	47	53	140	159	20	2	60	15.2	17.1	14.7	46	401.55	1	1	2	1
69	76	Saraswathi	1	1	3765	38.2	1	2	2	2	25	2	65	145	2	9.9	1	2	1	3	1	48	58	132	160	20.2	2	60.6	15.1	16	14.5	43.5	388.55	1	1	2	1
70	77	Vetriselvi	1	2	3040	38	1	2	2	2	28	2	97	157	2	10.4	1	2	1	3	1	58	47	155	156	19.5	2	58.5	10.1						2	2	1
71	78	Manjula	2	1	3490	38.1	1	2	2	2	26	2	65	153	2	10.4	1	2	1	3	1	54	48	154	150	15	2	45	13.2		9.7	28	107.34	1	2	2	1
72	79	Thayaluni	2	2	2200	35.5	1	1	2	1	25	2	68	144	2	10.9	1	2	1	2	1	57	49	159	148	19	2	57	6.9		13	39	209.12	1	2	2	1
73	80	Mathina bakam	1	1	3500	41.5	1	2	2	2	36	2	65	152	3	11	2	2	1	2	1	53	52	149	137	18.2	2	54.6	7.9		13.9	41.7	388.87	1	2	2	1
74	81	Selvi	1	1	2700	36.5	1	1	1	2	32	2	60	148	2	9	1	2	1	3	1	52	51	144	122	17.9	2	53.9	8.1		12.9	38.9	209.99	1	2	2	1
75	82	Anitha	1	1	3600	39.4	1	2	1	1	20	2	65	153	2	10.5	1	2	1	3	1	51	42	155	143	18.1	2	54.3	7.2		13.6	40.9	378.93	1	2	2	1
76	83	Samdhanibakam	1	2	3500	40.1	1	2	1	2	29	2	56	148	2	9.6	1	2	1	3	1	45	41	145	154	17.8	2	53.1	11.1		12.8	37	259.56	1	2	2	1
77	84	Rajalakshmi	1	1	3520	38	1	2	1	1	23	2	60	156	3	11	2	2	1	3	1	46	43	154	146	20	2	60	9		14	42	399.67	1	2	2	1
78	85	Lavanya	2	1	2980	36.6	1	1	1	1	20	2	72	152	2	10.8	1	2	1	3	1	49	47	160	135	20.3	2	60.9	15.8	15.8	14.2	42.6	180.87	2	1	2	1
79	86	Vijayalakshmi	2	1	3300	38.2	1	2	1	2	27	2	72	161	2	10.2	1	2	1	4	1	47	49	156	124	17.6	2	52.8	8.9		13.2	39.9	211.42	1	2	2	1
80	87	Kavitha	2	1	1800	36.5	2	1	1	1	21	2	64	149	2	9.6	1	2	1	3	1	51	48	145	142	18.2	2	54.6	8.2						2	2	1
81	88	Kanikeshwari	1	1	3300	40.2	1	2	1	2	23	2	65	158	2	10.2	1	2	1	4	1	42	50	147	153	19	2	57	7.5		14	42	345.22	1	2	2	1
82	89	Vanipriya	1	2	2650	37.5	1	2	1	1	24	2	72	154	2	10.8	1	2	1	3	1	44	51	135	155	19.5	2	59.2	6.8		14.5	43.5	245.78	1	2	2	1
83	90	Subashini	1	2	3315	37.4	1	2	2	2	27	2	72	154	3	11.2	2	2	1	2	1	53	53	153	159	18.9	2	56.7	5.4		14	42	189.57	1	2	2	1
84	91	Dhanalakshmi	1	2	3560	38.3	1	2	2	2	23	2	60	156	2	9.5	1	2	1	3	1	52	54	149	154	17	2	51.3	4.9		12.9	38.7	254.33	1	2	2	1
85	92	Nandhini	2	2	2310	36	1	1	2	1	23	2	68	154	2	10.8	1	2	1	3	1	46	56	159	132	19.2	2	56.7	4.5		13	39	311.23	1	2	2	1
86	93	Usha	1	1	3725	38	1	2	2	1	28	2	70	151	3	11.2	2	2	1	4	1	47	53	160	149	20	2	60.2	11.6		14	42	289.34	1	2	2	1
87	94	Sarala	1	1	3250	37.5	1	2	2	1	34	2	81	154	3	13.6	2	2	1	3	1	50	52	130	151	19.1	2	57.3	13.1		13.7	41.1	355.63	1	2	2	1
88	95	Narmadha	2	2	2940	38.4	1	2	2	2	22	2	75	146	2	10.5	1	2	1	3	1	55	49	143	139	18.6	2	55.8	12.1		13.2	39.6	289.85	1	2	2	1
89	96	joyvinolia	2	1	2570	39.1	1	2	2	2	28	2	63	156	2	10	1	2	1	3	1	56	47	148	147	17.9	2	53.7	5.9						2	2	1
90	97	Radha	2	2	2880	38.2	1	2	2	1	29	2	58	153	3	12	2	2	1	4	1	58	42	137	158	16.9	2	50.7	6.1		12.1	36.3	192.85	1	2	2	1
91	98	rukshana	1	1	3050	38	1	2	2	2	22	2	70	162	3	11	2	2	1	4	1	54	43	129	152	20.2	2	60.6	4.2		14.2	42.6	198.57	1	2	2	1
92	99	Farhadeba	1	2	2960	38	1	2	2	2	27	2	65	136	2	9.8	1	2	1	2	1	52	40	159	148	17	2	51	7.8		11.2	38	135.71	1	2	2	1
93	100	Deepa	1	1	3170	39.2	1	2	2	2	28	2	55	160	2	10	1	2	1	3	1	55	45	157	144	18	2	54	7.5		12.5	37.5	284.55	1	2	2	1
94	101	priya	2	2	2750	40.5	1	2	1	2	20	2	72	162	3	11.5	2	2	1	3	1	50	45	149	149	18.9	2	56.3	6.5		13.2	40.1	355.77	1	2	2	1
95	102	Aathibarasakthi	2	1	3030	41.2	1	2	1	1	30	2	64	152	2	9.8	1	2	1	3	1	56	45	129	158	18	2	54	7						2	2	1
96	103	Zareena	1	2	3200	37.5	1	2	1	2	22	2	70	155	2	9.7	1	2	1	2	1	56	47	158	150	17.4	2	52.3	8.1		12.9	38.7	390.85	1	2	2	1